

**THE STUDY OF OCCUPATIONAL RISK
FACTORS AND INTERVENTIONS FOR
BAKER'S ALLERGY AND ASTHMA AMONG
SUPERMARKET BAKERY WORKERS**

By

Roslynn Baatjies

Thesis presented for the degree of

Doctor of Philosophy

in the School of Public Health and Family Medicine

University of Cape Town

August 2013

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Supervisor: Professor Mohamed Fareed Jeebhay

Co-supervisors: Professor Dick Heederik and Dr Tim Meijster

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) in the School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town. The work on which this thesis is based is original research and has not, in whole or in part, been submitted for another degree at this or any other university. The contents of this thesis are entirely the work of the candidate, or in the case of multi-authored published papers, constitutes work for which the candidate was the lead author. The contribution of the candidate to included multi-authored papers is further delineated in the preface to the thesis and in the introduction to each included paper as appropriate.

Roslynn Baatjies

August 2013

ABSTRACT

Background: Baker's asthma is the most serious manifestation of occupational allergy among bakery workers. It is caused by IgE-mediated sensitisation and subsequent allergic reaction in the airways to specific occupational airborne allergens in flour or baking ingredients. Major aims of this study were to:

- characterise asthma phenotypes and environmental exposure to flour allergens among bakers and modifying factors;
- study associations between phenotype and environmental exposure and identify potential modifying factors of this association;
- determine the effectiveness of specific interventions in reducing exposure and the risk of sensitisation or allergic respiratory disease.

Methods: A cross-sectional study was conducted among 517 bakery workers employed in 31 supermarkets. Health outcomes were assessed using a standardized questionnaire, immunological tests (sIgE, sIgG), methacholine challenge test and fractional exhaled nitric oxide (FeNO). Exposure assessment conducted pre- and post-intervention entailed determination of inhalable concentration of particulate mass and specific allergen levels. The intervention employed a group-randomised design to evaluate dust control measures.

Results: Prevalence of probable occupational asthma (POA, 13%) was higher than atopic (AA, 6%), non-atopic (NAA, 6%) and work-aggravated asthma (WAA, 3%). Sensitisation to flour allergens was a major determinant of elevated FeNO among bakers. Bread bakers had the highest dust particulate (mean = 1.33 mg/m³) and allergen exposures. Exposure-response relationships followed a bell-shaped curve, with the prevalence of IgE- sensitisation, allergic symptoms and POA, increasing up to 10-15 µg/m³ of airborne wheat allergen concentrations before declining. The association

for IgE sensitization was not modified by IgG4 to wheat. The overall effect of the intervention revealed a 50% decrease in mean flour dust, wheat allergen and rye exposures in bakeries.

Conclusion: Occupational asthma is the most common phenotype among supermarket bakery workers, with sensitisation to cereal flour allergens being the main determinant of allergic airway inflammation. The bell-shaped exposure response relationship is not modified by the presence of blocking antibodies and is probably due to a healthy worker effect. The multi-pronged intervention strategy was effective in reducing airborne flour dust and allergen levels. It is recommended that further studies investigate the long term health impact of these interventions in reducing the disease burden.

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PREFACE

This thesis includes published papers, as per general provision 6.7 in the General Rules for the Degree of Doctor of Philosophy (PhD) of the University of Cape Town, and with the approval in 2013 of the University Doctoral Degrees Board. The following five papers are formally included as part of the thesis:

1. Baatjies R, Lopata AL, Sander I, Raulf-Heimsoth M, Bateman E, Meijster T, Heederik D, Robins TG, Jeebhay MF. **Determinants of asthma phenotypes among supermarket bakery workers.** European Respiratory Journal 2009; 34(4):825-833.
2. Baatjies R, Meijster T, Lopata AL, Sander I, Raulf-Heimsoth M, Heederik D, Jeebhay MF. **Exposure to flour dust in South African supermarket bakeries: Modeling of baseline measurements of an intervention study.** Ann. Occup. Hyg 2010; 54(3): 309–318
3. Baatjies R, Jeebhay MF. **Sensitisation to wheat is a major determinant of elevated exhaled nitric oxide in bakers.** Occup Environ Med, 2013;70(5):310-316
4. Baatjies R, Meijster T, Heederik D, Jeebhay MF. **Exposure-response relationships for wheat allergen exposure and asthma.** *Submitted to Occupational and Environmental Medicine*
5. Baatjies R, Meijster T, Heederik D, Sander I, Jeebhay MF. **Effectiveness of interventions to reduce flour dust exposure in supermarket bakeries.** *Submitted to Allergy*

The contribution of the candidate to each paper is outlined in the introduction to each paper. The candidate was the lead author for each paper, prepared all datasets for the analyses, conducted all the analyses and drafted all versions of the manuscripts. The candidate was responsible for circulating the manuscripts to co-authors, reviewing co-author comments and suggestions before integrating them into the manuscript as appropriate. All co-authors critically reviewed and approved the submitted manuscripts prior to submission.

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CHAPTER 1

INTRODUCTION

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1.1 INTRODUCTION

Occupational asthma is emerging as a common occupational lung disease in South Africa.¹ Recent reviews suggest that the median proportion of adult cases of asthma attributable to occupational exposure is approximately 18%.² Occupational asthma caused by allergy to proteins from cereal grains is one of the most common types of occupational asthma (OA) worldwide and its prevalence does not appear to be declining.³ Baker's asthma is the most serious manifestation of occupational allergy among bakery workers, which develops following inhalational exposure to flour dust allergens encountered in the work environment.⁴ Less severe types of baker's allergy are rhinitis, conjunctivitis and skin reactions such as urticaria.⁴

In the last decade there have been major changes in the baking industry in South Africa with a substantial decline (50%) in industrial plant bakeries and a four-fold increase in franchise bakeries (retail bakeries operating in-store bakeries, biscuit, pie and pizza outlets). In-franchise employment as a proportion of all employment in the baking industry has therefore doubled during this period.⁵ It is estimated that these bakeries provide job opportunities for more than 50% of the 45 000 bakers employed in 8000 baking units in South Africa. This shift in production practices has resulted in a changing risk profile for workers in the bakery industry.

In the Western Cape an increasing number of confirmed cases of baker's allergy and asthma has been diagnosed by the Occupational Medicine clinic at Groote Schuur hospital during the past decade. These incident cases arose from a particular supermarket chain, which sparked heightened interest in a large scale investigation of occupational allergy and asthma to flour dust among bakery workers employed in this company. It emerged that more than 10% of bakers had been redeployed from their jobs as bakers as a result of being diagnosed with baker's asthma. This represented a substantial loss of skilled bakers to the labour market in general and this

particular company in particular, since these jobs are difficult to replace due to the years of experience and training required to become a competent baker.

The main research questions that were addressed by this investigation was to determine the extent to which occupational exposure to various allergens constituted a risk to the health of bakery workers in this supermarket chain store. This was premised on the knowledge that there were no studies in South Africa that had documented the levels of total inhalable dust and specific allergen concentrations (wheat, rye, fungal α -amylase). Secondly, while some information on the occupational risk factors (mainly work practices) associated with the development of baker's allergy and asthma had been studied in traditional craft and industrial bakeries globally, studies among supermarket bakery workers were scant. Importantly, no studies could be identified that had determined the effectiveness of specific focused interventions to reduce exposure to flour allergens and the associated risk of sensitisation and/or allergic respiratory disease among bakers. It was envisaged that the data generated from this current study would contribute to and inform preventive measures that could be implemented with a greater level of certainty for their proven effectiveness in reducing the disease burden among bakers in general and supermarkets in particular.

1.2 STUDY AIM

The aim of this study was to determine the risk factors for allergic sensitisation and asthma due to flour and dust allergens and to evaluate the effectiveness of practical preventative measures in reducing this risk among supermarket bakery workers in Cape Town.

1.3 OBJECTIVES OF THE STUDY

1. Determination of the prevalence of allergic sensitisation, disease outcomes (rhino-conjunctivitis, urticaria, asthma) associated with exposure to flour dust in supermarket bakeries, and related host factors associated with these outcomes.
2. Determination of the predictors of elevated fractional exhaled nitric oxide, an early inflammatory marker in allergic disease, and its correlation with ocular-nasal and asthma symptoms and specific IgE to flour dust allergens.
3. Characterisation of environmental exposure, high risk work processes/job types of workers and determinants of exposure variability in supermarket bakeries through measurement of total personal inhalable flour dust and specific airborne allergen concentrations (wheat, rye, fungal α -amylase).
4. Exploration of the nature of exposure-response relationships for environmental exposure to wheat flour dust allergens associated with allergic sensitisation and related disease outcomes.
5. Development and evaluation of the effectiveness of practical interventions to reduce exposure to airborne flour dust and associated allergens.

1.4 STRUCTURE OF THE THESIS

In **Chapter 2** the available literature on baker's allergy and asthma is reviewed. The following issues are discussed: history of baker's asthma, potential allergens and allergen sources, exposure assessment in bakeries, epidemiology of baker's allergy and asthma, environmental and host determinants of baker's allergy, exposure-response relationships, and preventative measures and intervention studies.

Chapter 3 documents the prevalence and determinants of different asthma phenotypes in supermarket bakery workers. While baker's asthma has been well described, various asthma phenotypes in bakery workers have not been comprehensively described. This chapter attempts to characterize the various asthma phenotypes in supermarket bakery workers in relation to host risk factors and self-reported exposure to flour dust (see Figure 1).

Chapter 4 presents the predictors of fractional exhaled nitric oxide (FeNO). Studies of the relationship between FeNO and baker's allergy and asthma are scant. This is the first detailed analysis of factors associated with changes in FeNO in bakery workers. The long-term objective of this dust control programme (beyond the scope of this thesis) is to use the baseline FeNO as one of the markers to assess the effectiveness of the interventions for new onset airway inflammation and asthma among workers following the implementation of the intervention in the long term (see Figure 1).

In **Chapter 5** the characteristics of inhalable flour dust, wheat, rye and fungal α -amylase allergen exposures are studied. This chapter describes the findings of the detailed exposure assessment of these bakeries so as to provide the baseline for the intervention study. The variability and the sources of variation for inhalable dust, wheat, rye and fungal alpha-amylase allergen measures of exposure are discussed, in order to identify high risk jobs and work processes that could be prioritised for intervention.

In **Chapter 6** exposure-response relationships are explored with specific reference to the allergens implicated and allergic disease endpoints. The nature of the exposure-response relationship for wheat allergen levels in relation to sensitisation, work-related symptoms and occupational asthma are described in detail. The possible role of IgG4 to wheat in this exposure-response relationship is also evaluated in order to explain the apparent non-linear pattern observed.

Chapter 7 presents the details of the group randomized intervention study to evaluate the effectiveness of different control measures that were designed to reduce airborne flour dust exposure in these bakeries.

Finally, **Chapter 8** presents a discussion on the most important findings of this study, potential biases and implications for the prevention of flour dust-related allergic respiratory disease in general and for supermarket bakeries in particular.

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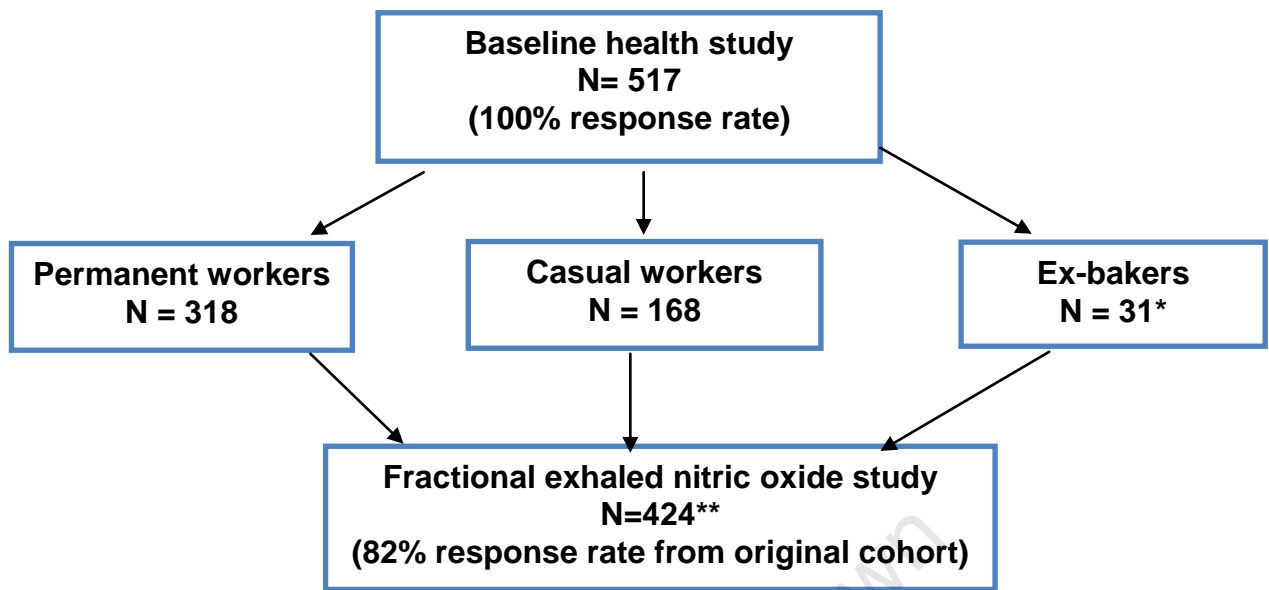


Figure 1. Schematic diagram of study population for the two cross-sectional health studies.

* The ex-bakers were recruited from medical records of the occupational medicine surveillance programme with the assistance of the occupational health nurse employed by the company. These bakers were commonly moved to other unexposed departments (such as administrative clerks, customer care consultants) within the supermarket and easily accessible for enrolment into the study.

** The second cross-sectional study was conducted on 424 of the 517 workers originally enrolled in the study of the 31 supermarket bakeries. At follow up, 3 years later, 93 workers from the original cohort were no longer working in the bakery and were not traceable for further evaluation.

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- ⁴ Houba R, Doekes G, and Heederik D. Occupational Respiratory Allergy in Bakery Workers: A review of the literature. *Am J Ind Med* 1998;34:529-546.
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CHAPTER 2

LITERATURE REVIEW

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2.1 BACKGROUND AND REVIEW OF THE LITERATURE ON BAKERY WORKERS

Asthma from cereal grains such as baker's asthma is one of the most common forms of occupational asthma, and its prevalence does not appear to be declining.¹ Ramazzini in 1700, wrote the first scientific report on baker's asthma.² It is only in the 19th century (1909) that allergic sensitisation by skin reactivity to wheat extracts was demonstrated in a baker with asthma. For the first time in 1929 de Besche introduced baker's asthma as an allergic disease.³ Baker's asthma is not only confined to bakers, since exposure to these allergens can result in the development of the disease and can be present in confectioners, pastry factory workers, flour millers and food processors.⁴ Exposure to cereal flours such as wheat and rye, but also enzymes have been reported to play an important role. Subsequent studies have identified several wheat flour proteins as allergens in sensitised bakers with asthma.^{5,6}

2.2 THE BAKING PROCESS AND HIGH RISK ENVIRONMENTAL EXPOSURE SETTINGS

Occupational exposure to flour occurs mainly in occupations such as bakeries, flour mills, food-producing and processing industries, and related industries such as enzyme-producing and baking-ingredient industries. Many of these bakeries are located in supermarkets or are traditional small scale craft bakeries. Besides bread products such as cakes, biscuits and pastry are produced. Flour, but also yeast, spices and additives are used as main ingredients. The production process includes activities such as sifting of flour, making dough, cutting and shaping, baking, cooling and storing. Ingredients that are potentially allergenic are wheat flour, rye flour, fungal α -amylase, enzymes, soya flour, malt flour, gluten and sesame seeds (see Appendix 1).

Results of exposure studies demonstrate that workers at the front end of the process of baking process such as bakers and dough makers generally have the highest 8-hr average dust exposures.^{7,8} Activities like sieving, weighing and mixing are associated with high dust exposures.⁹ Furthermore cleaning operations, bread and roll-production also give rise to high exposures.¹⁰ Peak exposures are caused by dusting during dough forming (to prevent dough adhesion to surfaces) or by adding ingredients into the dough mixer. The relationship between dust and wheat antigen exposure varies considerably, depending on the specific bakery occupation, the size of the bakery, and the type of product produced by the bakery.¹¹

2.3 CONSTITUENTS OF FLOUR DUST AND POTENTIAL ALLERGEN AND THEIR SOURCES

Flour and its additives contain many potential allergens, which include components of wheat flour as well as flour contaminants such as mites, weevils and moulds.¹² Well-known high-molecular-weight sensitisers are wheat proteins and baking additives such as enzymes (e.g. *Aspergillus*-derived) fungal α -amylase.¹³ A recent review by Quirce (2013), reported that proteins represent 10-15% of wheat grain, and that the salt-soluble fractions, viz. albumins and globulins, comprise only 15-20% of the total protein.¹ The general consensus is that wheat flour and fungal α -amylase are usually the most important allergens (except in countries such as Germany where the widespread use of rye makes it a more common allergen). With increasing modernisation and innovations in the baking industry over the last few decades, and the introduction of new ingredients the list of causative agents in baker's asthma has also expanded. Table I lists potential allergen sources, including non-flour related products, associated with exposure among bakery workers.

Table 2.1 Potential allergen sources associated with baker's allergy and asthma

<p>Cereal Flours Wheat Rye Barley Cereal malt flour Rice flour</p> <p>Non cereal flours Soybean flour Buckwheat Lecithin (from soybean)</p> <p>Baking additive enzymes α-amylase Glucoamylase (Hemi) cellulase Protease Xylanase Papain Glucose oxidase</p> <p>Moulds and Yeast Aspergillus, Alternaria Baker's yeast</p> <p>Other additives Egg material yolk Egg white Almond, hazelnuts Cacao Milk powder Sesame seeds Chocolate</p> <p>Insects Storage mites Grain weevil Flour beetle Cockroach Flour moth</p>
--

2.4 EPIDEMIOLOGY OF ALLERGIC SENSITISATION AND ASTHMA ASSOCIATED WITH FLOUR DUST

It is well documented that exposure to flour dust increases the risk of allergic sensitisation and lung diseases, particularly occupational asthma.

a) Allergic Sensitisation

Cereals

Cereal flours, in particular wheat flour and other cereal flours such as rye flour and barley flour have been documented as important allergens causing allergic diseases in bakery workers.⁴ Wheat flour protein allergens are reported to be responsible for 60% to 70% of all cases of workers reporting work-related respiratory symptoms.⁵ The prevalence of sensitisation to wheat flour has been measured in epidemiologic studies, using either skin prick testing or specific serum IgE-antibodies. The review by Houba et al¹⁴ reported the prevalence of sensitisation to wheat flour ranging from 5 – 28%, in epidemiological studies from 1967 – 1998. More recent studies show the incidence of sensitisation to flour is estimated to be between 2.2 – 4.2% per person year.^{1,15} However, most of these studies were conducted in large industrial bakeries or milling plants. With specific reference to supermarket bakeries, a British study reported the IgE reactivity to flour (11%) of bakery employees, which was similar to small Italian bakeries (12%).^{8,16} However, studies in craft bakery workers, have reported a much higher prevalence of 24%.¹⁷ The majority of bakers with workplace-related asthma or rhinitis are sensitized to wheat or rye flour. One such study of baker's asthma reported that bakers with workplace-related respiratory symptoms showed mainly sensitisation to wheat flour (64%), rye flour (52%) and soybean flour (25%).¹⁸ It has also been shown that sensitisation precedes the onset of upper and lower airway symptoms, and asthma.¹⁹ However, Skjold et al²⁰ have reported

that the development of rhinitis and asthma-like symptoms in apprentice bakers were not always preceded by sensitisation to occupational allergens. This is contrary to the allergic march theory, which anticipates a sequence of sensitisation followed by nasal symptoms that may progress to asthma. This suggests that the mechanism underlying work-related respiratory symptoms can not solely be attributed to an IgE mediated pathway.

Enzymes

Exposure to fungal α -amylase has been reported as an important risk factor in British bakeries and flourmills for the development of occupational asthma.²¹ Fungal α -amylase is routinely added to flour to speed up the baking process and improve bread quality. These enzymes modify the viscosity of the dough, volume and colouring of the bread product, and lengthen the shelf life of bread. First reports of enzyme-related respiratory morbidity in bakers were in the early 1980s. Since then, several case reports have been reported of bakers' asthma caused by this enzyme, often in the absence of specific IgE to cereal allergens.^{22,23,24} The prevalence of sensitisation varies from 2-16% for fungal α -amylase.⁷ An epidemiologic study in British supermarket bakeries found that 5% of the workers had positive skin prick test to α -amylase whereas an Italian craft bakery study reported a slightly higher prevalence of 7.5%.^{8,25} Vanhanen et al²⁶ in their study on enzyme exposure and enzyme sensitisation in the bakery industry found that 8% of workers in bakeries, 5% in flourmills, and 3% in crispbread production were sensitized to enzymes such as cellulase and xylanase. The incidence of sensitisation to fungal α -amylase is estimated to be 25 cases per 1 000 pyrs (2.5%).¹⁵ Baur et al in his studies relating to α -amylase exposure found that 24-55% of bakers with respiratory symptoms attending medical services, were sensitized to α -amylase.^{27,28,29}

Storage mites

Wheat flour in bakeries can be contaminated with storage mites, and allergens from storage mites have been suggested as another cause of allergic symptoms in bakery workers.³⁰ A number of epidemiologic studies show a high prevalence of sensitisation to storage mites (*Acarus siro*, *Glycyphagus domesticus*, *Lepidoglyphys destructor*, *Tyrophagus longior*, and *Tyrophagus putrescentiae*) in bakery workers varying between 11-33%,^{16,25,26} however Tee et al³¹ suggested that cross-reactivity with house dust mite maybe the main reason for immunological reactivity observed in bakery workers.

Other potential allergen sources

While exposure to cereal flours such as wheat and rye, as well as enzymes such as fungal α -amylase has been well documented as major allergens in causing baker's asthma, other allergens have also been reported. Sensitisation to soybean flour has been reported in 3% of bakers.¹⁴

Specific allergens identified

With increasing technology available over the years in the investigation of baker's asthma, purified wheat proteins either in natural or recombinant forms have been implicated in the pathogenesis of baker's asthma. Sander et al⁵ identified more than 100 IgE-binding protein spots associated with baker's asthma, and demonstrated reactions in sera from sensitized bakers to many of these antigens. Weichel et al³² demonstrated that wheat thioredoxin hb (Tri a25) is a novel cross-reactive allergen that may contribute to the symptoms of baker's asthma, while Palacin et al³³ reported that recombinant wheat lipid transfer protein (Tri a 14) as being an important allergen and a potential tool for baker's asthma diagnosis. Lehto et al³⁴

demonstrated reactions to α -amylase inhibitor, peroxidase, thaumatin-like protein, and to lipid transfer protein 2G. More recent reviews by Salcedo et al³⁵ and Quirce¹ summarised these studies which have identified several other salt-soluble proteins (albumins and globulins) such as cereal α -amylase/trypsin inhibitors, peroxidase, thioredoxin, nonspecific lipid transfer protein, serine proteinase inhibitor, and thaumatin-like protein; salt-insoluble storage proteins (prolamins, namely, gliadins and glutenins); and recombinant allergens as the allergens associated with baker's asthma. However, the review highlighted important limitations of these studies including the lack of comparability between recombinant and natural allergens in wheat flour, low reactivity rates and a low number of patients studied.³⁵

b) Respiratory symptoms and asthma

Rhinitis

In many epidemiological studies among bakery workers, ocular-nasal symptoms as well as allergic symptoms are reported, which often precedes the development of work-related asthma symptoms and baker's asthma. Studies among Swedish trainee bakers estimated incidence rates of 29.4 cases per 1 000 person-years for rhinitis,^{36,37} whilst a British study reported incidence rates of work related ocular-nasal symptoms of 118 per 1000 person-years.¹⁵ Various epidemiological studies have consistently reported that rhinitis is a significant risk factor for adult-onset asthma, for both work-related and non-work-related disease outcomes and that the appearance of ocular-nasal symptoms could be used to identify workers at increased risk of developing occupational asthma.^{38,39,40} Previous studies have shown that 11.5% of subjects with occupational rhinitis develop occupational asthma, and specifically 11.6% of these individuals are exposed to flours and grains.³⁸ Co-morbid rhinitis or rhino-conjunctivitis has been reported in a

greater proportion (45-90%) of subjects suffering from IgE-associated OA and has been attributable to various sensitizers including flour dust.⁴¹

Asthma

There are various phenotypes of work-related asthma that have been described including occupational asthma and work-aggravated asthma. The diagnosis of baker's asthma (occupational asthma) depends on a history of work-related asthma symptoms, specific sensitization to bakery allergens and variability in lung function associated with exposure to flour dust. Studies conducted among bakery workers have documented a prevalence of respiratory symptoms varying between 5% and 21%.^{12,16,25,26} The reported prevalence of bronchial hyper-responsiveness ranges between 25% and 40%.^{42,43,44}

The positive association of sensitization to bakery allergens and work-related symptoms in baker's asthma has been further demonstrated in a nested case-control of bakery students,⁴⁵ as well as in an industrial and small bakery setting using a referent population from the petrochemical industry.⁴⁶ Quirce et al⁴⁷ demonstrated that a positive skin prick test to an occupational allergen and nonspecific bronchial hyper-responsiveness (NSBH) correlated with a positive specific inhalation test to flour dust. The authors concluded that that a work-related history and NSBH together with specific sensitization is highly predictive of occupational asthma. Specific inhalation challenge test is still the gold standard for the diagnosis of occupational asthma caused by flour. Specific inhalation challenge tests performed in 160 bakers with suspected baker's asthma, demonstrated positive test for early asthma in 42 subjects (26%) and for late/dual asthma in 18 (11%).⁴⁸

The prevalence of probable occupational asthma in epidemiological studies ranges between 4-13% in various studies of industrial bakeries in which a

similar definition of occupational asthma (bronchial hyper-responsiveness and sensitivity to flour) was used.^{8,49} Incident studies of baker's asthma have reported rates of 3 - 41 cases per 1 000 person-years.^{15,37} A recent study the incidence of baker's asthma among young bakers reported a range from 0.3 to 2.4 cases per 1,000 person-years.⁵⁰

2.5 EXPOSURE ASSESSMENT STRATEGIES FOR CHARACTERISING EXPOSURE TO FLOUR DUST

When investigating the association between exposure to flour dust and the development of sensitisation and/or symptoms and disease, an accurate quantitative estimate of exposure is needed for each worker. In addition it has been demonstrated that exposure reductions are difficult to evaluate and biased when using subjective methods, and exposure survey should therefore be an integrated part of studies on the prevention of occupational asthma.⁵¹ The quantitative exposure assessment is of utmost importance in evaluating the risk for the development of baker's asthma.¹

Individual versus group-based approaches

Grouping strategies based on job titles

Most exposure assessment studies among bakery workers, have employed grouping strategies based on job titles. In earlier studies, investigators explored the determinants of variability in inhalable dust exposures. The authors concluded that using occupational titles of bakery workers were considered as the most important determinant of dust exposure and the best way to categorise bakery workers into exposure groups.^{52,53} Job title explained 43-50% of the variability in dust exposure levels in these studies. Studies investigating the variability in wheat allergen exposure, also demonstrated that job title was the most important determinant of variability

in exposure levels. Studies have also demonstrated significant differences in inhalable dust and wheat allergen exposure ascribed to the type of end-products.^{52,54} Furthermore, it has been shown that a grouping strategy based on a combination of job and type of bakery resulted in high contrast in exposure with elasticity of 0.75, 0.81 and 0.77 for inhalable dust, wheat allergen and α -amylase allergen respectively.⁵⁴ However, the authors concluded that for exposure to inhalable, wheat allergens and α -amylase allergens, job title could be used on its own as an important explanatory variable since it lead to comparable contrast in average exposure levels. Elms et al⁵⁵ also demonstrated that job categories are useful when they investigated exposure levels to inhalable dust and fungal α -amylase. In their study marked differences were observed between highly exposed workers such as mixers and weighers and confectionery and other bakery workers.

Task-based sampling

A few studies have been conducted that have focussed specifically on the influence of task and production variables on exposure levels. Bakery workers generally perform several short and repeated tasks at different production points that may influence their exposure during a work shift. Traditional exposure assessment strategies based on 8-h exposure measurements [time-weighted average (TWA) exposure] may not always be sensitive enough to identify (task) specific determinants of exposure, including the effect of control measures. Nieuwenhuijsen et al¹⁰ used task-based sampling as a strategy to quantify exposure in bakeries, and demonstrated that exposure levels for bakery workers to a large extent were determined by peak exposures that could be associated with specific work activities. The investigators showed that the highest dust exposure was found during cleaning operations, although bread- and roll production were also identified as tasks with considerable flour dust exposure. Studies in Dutch bakeries have evaluated peak exposures in the flour processing industry. The investigators showed that exposure to flour dust is primarily

caused by short-term, sometimes very intensive, peak exposure tasks, and can have a substantial effect for an individual worker's exposure (Figure 1). This study also provided information on the potential impact of specific intervention strategies directed at tasks associated with high exposure.⁵⁶

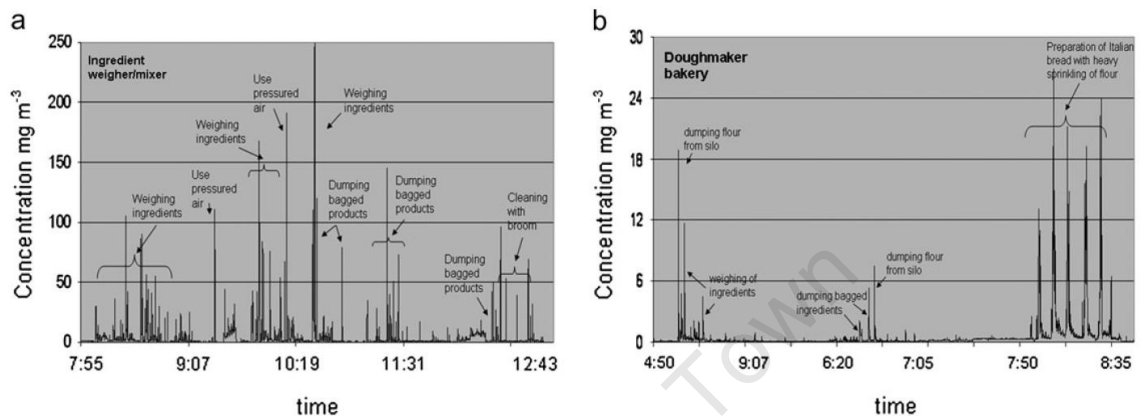


Figure 2.1 Plots from (partial) real-time measurements showing specific labelling of type of peak exposure for two different jobs reproduced from (Meijster et al).⁵⁶

Allergen characterisation of flour dust

The understanding and measurement of the exposure to flour dust and other allergens in bakeries is of importance when analysing the risk for asthma, and in studying exposure-response relationships.⁴ In earlier studies exposure assessment in bakeries were based only on measuring inhalable flour dust exposure, since methods for measuring allergen exposure in bakeries were not available. However, wheat flour and fungal alpha-amylase have subsequently been documented as important allergens, and therefore the quantification of these allergen exposures are essential. Valid and reliable techniques to measure these allergens are essential tools for controlling allergen exposure levels and reducing the incidence of occupational respiratory disorders.

Various allergen quantification methods have been described: a human IgE inhibition RAST⁵⁷, a rabbit IgG inhibition radioimmunoassay (RIA)⁵⁸ and a human IgG4 inhibition enzyme immunoassay (EIA).¹¹ These assays have been used in studies that demonstrated significant exposure-response relationships between the levels of allergen exposure and the risk of wheat allergy.^{59,60} The Measurement of Occupational Allergen Exposure project (MOCALEX) compared immunoassay methods for assessment of occupational bio-allergen exposure in the workplace, including bakery allergens, for purposes of standardising airborne measurements. The researchers concluded that the rabbit IgG inhibition EIA was the most convenient assay for routine measurements of full-shift airborne wheat samples in medium- to high-exposure bakeries and the flour mill environment.⁶¹

Recently, several assays have been refined for measuring personal allergen exposure levels in bakery environments to bakery allergens such as rye flour allergens and enzymes such as fungal alpha-amylase. Fungal alpha-amylase allergens have been measured using a sandwich enzyme immunoassay with monoclonal mouse antibody antibodies for capture and affinity-purified polyclonal rabbit IgG antibodies for detection as described by Sander et al⁶² and by Bogdanovic et al.⁶³ Rye flour allergens have been quantified using a rabbit (NewZealand White) immunized with an allergenic rye seed extract and a two-sited assay developed after Protein G purification of the coating antibodies and antigen-affinity purification and biotinylation of the detection antibodies.⁶⁴

Using these techniques subsequent studies have demonstrated the importance of quantifying allergen concentration of flour dust, and showed that dust levels may only partially correlate with the actual allergen concentration.⁵⁸ This has highlighted the issue whether dust levels are a valid exposure parameter in occupations where IgE-mediated allergies predominate. Studies conducted on wheat antigen content of inhalable dust

have therefore concluded that exposure measurements carried out for the purpose of managing occupational risks of aeroallergen exposure in bakeries should use analytical techniques that can directly measure antigen exposure.⁶⁵ This was based on the finding that the wheat antigen content of bakery dust varied greatly between Canadian and Dutch bakeries, with bakery dust from the Canadian study having much higher wheat antigen content. This inter-study difference in the wheat antigen content of bakery dust was by far the most significant in undermining the validity of the use of dust levels as a surrogate measure of wheat antigen content. Houba et al¹¹ also demonstrated significant differences in the dust and allergen exposure measures in the comparison of exposure levels by job title. In this study, authors observed small difference in dust levels among occupational titles with exposure levels below 1mg/m³. However, wheat antigen exposure levels in these occupational titles varied from 77 – 992 ng/m³, the former being 13 times higher than the latter. Studies measuring airborne alpha amylase levels also showed levels varying from 0 – 40 ng/m³ depending on the type of bakery and job title, but having a poor correlation with inhalable flour dust levels (0.19).⁶⁶

Industrial hygiene sampling techniques

The first personal samples measurements in bakeries were documented by Hartmann (1986). Different exposure data and techniques used for personal exposure measurements are presented in Table 2. It is evident that different sampling strategies and sampling techniques have been used in these studies. It is likely that these methods have measured the inhalable fraction with different levels of accuracy and precision. In the light of this, a collaborative European laboratory study compared the performance of these monitors and demonstrated that certain samplers such as the IOM, GSP and PAS-6 measured inhalable dust levels fairly well.⁶⁷ A Nordic study of bakeries by Kruse et al⁶⁸ of four inhalable samplers viz. PAS6, IOM, GSP and Button demonstrated that the precision of the GSP and IOM was inferior

to the PAS6, and concluded that the PAS6 provided the best estimate for inhalable flour dust sampling in bakeries.

Exposure levels of dust and flour allergens in bakeries

Dust levels

The inhalable flour dust concentration for the different occupational titles across studies are outlined in Table 2. The results demonstrate that workers at the front end of the baking process (dough makers, bread formers) have the highest 8-hr average dust exposures (average inhalable dust exposures of 2 - 9 mg/m³). For oven workers the exposure levels ranged from 0.6 – 3.2 mg/m³. Bakery workers with tasks that involved slicing and packaging of bread or other products had exposure levels around 1 mg/m³.

Nieuwenhuijsen et al⁵² conducted a study among bakeries and flour mills and divided workers into various exposure groups, which included dispensing/mixing, bread production and confectionery. Among the bakeries, the groups with the highest exposure levels were confectionery (dough brake), dispensing/mixing, and bread production with exposure levels of 6.1 mg/m³, 3.8 mg/m³, and 1.4 mg/m³ respectively. A study conducted by Burdorf et al⁶⁹ employed a task-based grouping strategy to evaluate exposure to flour dust. Workers were assigned to the following a priori exposure groups: dough makers, bread-formers, confectionery workers, oven workers and packers. The investigators found a clear hierarchy in geometric mean exposure levels among bakery workers, in descending order of exposure: dough makers (5.5 mg/m³), bread-formers (2.7 mg/m³), oven workers (1.2 mg/m³), packers and confectionery workers (0.5 mg/m³) (table 2).

Wheat allergen

Studies of exposure to wheat flour allergens is summarised in Table 3. Wheat flour allergens exposures differ significantly among various occupational titles and/or exposure groups. For personal wheat antigen exposure similar trends were observed as illustrated in personal inhalable dust concentrations between various job titles and exposure groups. The highest exposure levels were found among dough makers and workers involved in bread production. Bulat et al⁷⁰ found the highest exposure levels among traditional bakeries in bread production ($22.33\mu\text{g}/\text{m}^3$) as well as bread and pastry production ($14.48\mu\text{g}/\text{m}^3$). The personal wheat flour allergen exposures of these two groups were significantly higher than in the other three groups ($p<0.01$). Furthermore, the wheat flour allergen exposures were significantly higher among bread-producing workers in comparison to packers ($p<0.01$) in industrial bakeries.

Fungal α -amylase

A British study reported considerable differences between levels of exposure to fungal α -amylase between exposure groups, with workers employed in dispensing and mixing areas having the highest exposure ($39.7\text{ ng}/\text{m}^3$) (Table 4). Houba et al⁶⁶ found the highest fungal α -amylase exposures among dough makers producing crispbakes (GM $18.1\text{ ng}/\text{m}^3$), followed by dough makers in wheat bread production (GM 0.8), as well as bread and mixed bakers in small bakeries ($0.2 - 0.3\text{ ng}/\text{m}^3$). Another British study found that mixers and weighers had significantly higher levels of fungal α -amylase ($3.2-29.1\text{ ng}/\text{m}^3$), compared to other job categories ($p<0.01$).⁵⁵ This trend was also identified by Nieuwenhuijsen et al²¹ and Vanhanen et al⁷¹ reporting the highest levels of fungal α -amylase exposure in dough making areas of the bakery. Similarly, it has been demonstrated that bread production

workers also had the highest exposure (0.61 ng/m^3), compared to packaging workers (0.15 ng/m^3).⁷⁰

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Table 2.2 Exposure characterisation of dust measurements in bakeries according to occupational titles

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM or AM*	GSD or SD*	Range
Hartmann (1986)	3	NR	31	31	All	NR	NR	0.2 -19.8
Masalin et al (1988)	NR	NR	29	29	All	NR	NR	0.1-8.8
Musk et al (1989)	Full-shift	Casella or Millipore (total dust)	79	10 16	Doughmakers Oven staff	2.7 1.7	NR NR	0.6-14.1 0.0-37.6
Jeffery (1992)	Full-shift	7-hole or Casella (inhalable/total dust)	68	3 16	Weighing/mixing Dividing/moulding	8.6 4.7	2.3 2.0	3.3-15.8 1.6-19.1
Jauhiainen et al (1993)	4-7	3-piece cassettes (total dust)	20	13	Making of dough Making of bread	4.6 ^b 2.3 ^b	3.6 ^b 0.9 ^b	0.9-14.7 1.5-3.4
Kolopp-Sarda et al (1994)	NR	NR	10	10	All	4.9 ^b	9.1 ^b	NR
Bohadana et al (1994)	4	Millipore (total dust)	21	14 6	General baker Oven handler	3.4 ^b 1.1 ^b	3.7 ^b 0.9 ^b	0.7-8.7 0.5-2.7
Lillienberg and Brisman (1994)	Full-shift	IOM (inhalable)	29	6 3 10	Dough mixing Oven control Dough forming	7.5 ^b 3.2 ^b 2.5 ^b	5.4 ^b 1.7 ^b 0.8 ^b	NR NR NR
Burdorf et al (1994)	1-7	IOM (inhalable)	129	34 62 10	Dough makers Bread formers Oven workers	5.5 ^c 2.7 ^c 1.2 ^c	2.1 ^c 2.0 ^c 2.4 ^c	1.2-16.9 0.6-14.2 0.2-4.0

*N = total number of personal samples; n = number of samples taken in occupational title; AM = arithmetic mean; GM = geometric mean; SD = Standard deviation; GSD = geometric standard deviation;^b = concentration and standard deviation in AM and SD (all others GM and GSD); ^c = GM and GSD could be biased because of large variations in sampling time; ^d = sampling time varied from 2 to 4 hours but several consecutive personal samples were taken to cover the whole working shift; ^e = Median level of exposure, NR = Not reported

Table 2.2 Exposure characterisation of dust measurements in bakeries according to occupational titles (continued)

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM or AM*	GSD or SD*	Range
Nieuwenhuijsen et al (1994)	Full-shift	7-hole (inhalable)	352	24 32	Dispense/mixing Roll production	5.0 2.4	2.5 2.5	1.4-86.0 0.4-21.1
Houba et al (1996a)	Full-shift	PAS-6 (inhalable)	546	105 66 27 81 20 132	Doughmakers All round staff Maintenance Oven staff Production managers Slicers, packers	3.0 0.9 0.7 0.6 0.6 0.4	2.3 NR NR 2.2 NR NR	0.4-37.7 0.1-26.8 0.3-5.5 0.1-5.1 0.1-4.9 0.1-2.8
Vanhanen et al (1996)	Full-shift ^d	Milipore (total dust)	30	7 10	Dough making Bread making	8.4 ^b 3.2 ^b	NR NR	3.0-18.8 1.2-5.5
Burstyn et al (1997)	Full-shift	7-hole (inhalable)	96	96	All bakers using flour	2.1	5.1	0.1-110
Elms J et al (2003)	Full-shift	IOM (inhalable)	117	13 3 29 21 5 8 9	Weigher Pastries Mixer Baker Confectionery Ovens Packer	11.4 ^δ 11.2 ^δ 7.6 ^δ 6.3 ^δ 4 ^δ 2.1 ^δ 0.8 ^δ	NR NR NR NR NR NR NR	2.4-26.3 2.5-13.3 1.0-36.8 <LOD-27.8 0.6-8.2 <LOD-18.0 <LOD-2.2

*N = total number of personal samples; n = number of samples taken in occupational title; AM = arithmetic mean; GM = geometric mean; SD = Standard deviation; GSD = geometric standard deviation; ^b = concentration and standard deviation in AM and SD (all others GM and GSD); ^c = GM and GSD could be biased because of large variations in sampling time; ^d = sampling time varied from 2 to 4 hours but several consecutive personal samples were taken to cover the whole working shift; ^δ = Median level of exposure, NR = Not reported

Table 2.2 Exposure characterisation of dust measurements in bakeries according to occupational titles (continued)

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM or AM*	GSD or SD*	Range
Bulat et al (2004)	Full-shift	PAS-6 (inhalable)	300	29	Bread production	2.10	2.42	0.30-13.30
				57	Pastry production	1.11	2.55	0.23-8.70
				22	Baker	1.06	3.61	0.17-8.52
				31	Packaging	0.56	2.09	0.22-2.17
Elms et al (2005)	Full-shift	IOM (inhalable)	208	108	Baker/dough brake	3.3	3.4	<LOD-47.0
				59	Mixer/siever	4.7	3.4	<LOD-30.6
				6	Cleaner	3.8	3.5	0.4-14.3
				35	Other	2.2	2.8	<LOD-30.8
Elms et al (2006)	Full-shift	IOM (inhalable)	195	100	Baker/table	3.3	NR	NR
				55	Mixer/siever	4.7	NR	NR
				6	Cleaner	3.8	NR	NR
				34	Other	2.2	NR	NR
Meijster et al (2008)	Full-shift	PAS-6 (inhalable)		30	Breadbaker	4.49	NR	NR
				4	Pastry maker	0.49	NR	NR
				16	Dough maker	1.82	NR	NR
				8	All baker	2.02	NR	NR
				1	Storage worker	2.32	NR	NR

*N = total number of personal samples; n = number of samples taken in occupational title; AM = arithmetic mean; GM = geometric mean; SD = Standard deviation; GSD = geometric standard deviation;^b = concentration and standard deviation in AM and SD (all others GM and GSD); ^c = GM and GSD could be biased because of large variations in sampling time; ^d = sampling time varied from 2 to 4 hours but several consecutive personal samples were taken to cover the whole working shift; ^e = Median level of exposure, NR = Not reported

Table 2.3 Exposure characterisation of wheat allergen measurements in bakeries according to occupational titles

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM	GSD	Range
Nieuwenhuijsen et al (1994)	Full-shift	Casella (inhalable)	495	24	Dispensing/mixing	228.7*	2.4	25.9-842.97
				32	Roll production	215.3*	1.8	71.1-1015.3
				9	Dough brake	208.5*	3.0	36.1-1912.7
				45	Bread production	176.6*	2.3	43.9-744.3
				36	Hygiene inside	148.6*	3.8	15.4-4506.3
Houba et al (1996a)	Full-shift	PAS-6 (inhalable)	449	76	Doughmakers	5,232	NR	33-252,407
				54	All round staff	992	NR	33-68,159
				17	Production managers	505	NR	33-74,614
				71	oven staff	322	NR	33-28,079
				20	Maintenance	242	NR	33-2,539
				109	Slicers, packers	77	NR	33-7,736
Bulat et al (2004)	Full-shift	PAS-6 (inhalable)	300	<i>Industrial bakery</i>				
				20	Baker	6.15*	3.57	1.5-100.3
				32	Packaging	2.79*	2.25	0.5-48.44
				<i>Traditional bakery</i>				
				30	Bread production	22.33*	2.97	1.9-171.23
				138	Bread and pastry	14.48*	3.75	0.46-205.9
				60	Pastry production	8.71*	4.16	0.58-150.7

Note: N = total number of personal samples; n = number of samples taken in occupational title; GM = geometric mean; GSD = geometric standard deviation

*Wheat allergen concentration in $\mu\text{g}/\text{m}^3$, NR = Not reported

Table 2.4 Exposure characterisation of fungal alpha-amylase allergen measurements in bakeries according to occupational titles

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM	GSD	Range
Houba et al (1997a)	Full-shift	PAS-6 (inhalable)	507	32	Doughmakers	0.8	5.14	<LOD-33.1
				35	All round staff	0.2	2.35	<LOD-14.3
				77	oven staff	0.2	1.45	<LOD-2.3
				119	Slicers, packers	0.2	1.44	<LOD-8.8
				27	Maintenance	0.2	1.33	<LOD-0.7
				20	Production managers	all < limit of detection (LOD)		
Nieuwenhuijsen et al (1999)	Full-shift	Casella (inhalable)	478	3	Dispensing/mixing	39.7	2.2	NR
				14	Hygiene (inside)	1.5	4.3	NR
				11	Roll production	1.0	5.3	NR
				23	Bread production	0.4	5.4	NR
				21	bread wrapping	0.1	1.3	NR
Elms J et al (2003)	Full-shift	IOM (inhalable)	117	13	Weigher	29.1 ^δ	NR	<LOD-1370
				29	Mixer	3.2 ^δ	NR	<LOD-123
				21	Baker	1.6 ^δ	NR	<LOD-185
				8	Ovens	1.5 ^δ	NR	<LOD-3.2
				9	Packer	1.4 ^δ	NR	<LOD-2.1
				3	Pastries	1.1 ^δ	NR	<LOD-1.5
				5	Confectionery	below limit of detection		

*N = total number of personal samples; n = number of samples taken in occupational title; GM = geometric mean; GSD = geometric standard deviation

^δ = Median level of exposure, NR = Not reported

Table 2.4 Exposure characterisation of fungal alpha-amylase allergen measurements in bakeries according to occupational titles (continued)

Study author (year)	Sampling Time (hours)	Sampling head (dust fraction)	N	n	Occupational title	GM	GSD	Range
Bulat et al (2004)	Full-shift	PAS-6 (inhalable)	300	29	Bread production	0.61	3.89	0.11-17.65
				20	Baker	0.47	7.19	0.11-36.16
				59	Pastry production	0.47	4.04	0.10-51.13
				32	Packaging	0.15	1.74	0.11-1.24
Elms et al (2006)	Full-shift	IOM (inhalable)	195	100	Baker/table	1.7	NR	NR
				55	Mixer/siever	NR	NR	NR
				6	Cleaner	NR	NR	NR
				34	Other	NR	NR	NR

*N = total number of personal samples; n = number of samples taken in occupational title; GM = geometric mean; GSD = geometric standard deviation

^δ = Median level of exposure, NR = Not reported

2.6 ENVIRONMENTAL RISK FACTORS AND EXPOSURE-RESPONSE RELATIONSHIPS FOR FLOUR DUST AND BAKER'S ASTHMA

There is consistent evidence that the risk of developing occupational allergy increases with allergen exposure.⁷² However, this exposure-response relationship is complex. One of the first studies showing an exposure-response relationship was conducted in 1989. In this study by Musk et al workers were ranked based on occupational title and were grouped based on "perceived dustiness", not on actual exposure. The authors demonstrated that sensitisation to wheat flour was more common among highly exposed workers using this definition of exposure (OR = 3.0; 95% CI 1.4-6.3).⁴²

In recent years, the evaluation of dose-response relationships has been greatly enhanced due to the development of immunoassay techniques for the quantification of airborne allergens in the workplace, the use of rigorous personal sampling techniques, and the implementation of prospective cohort study designs.⁷²

In earlier studies conducted using actual exposure measurements, the frequency of sensitisation to wheat flour and α -amylase increased with intensity of dust exposure as well as wheat allergen exposure.²⁵ A strong, positive association has been demonstrated between wheat flour allergen exposure and wheat-flour-specific allergic sensitisation.¹¹ Similarly a strong and positive association has been found between fungal alpha- amylase allergen exposure levels and specific allergic sensitisation.⁷³

These studies provided the first evidence supporting a dose-response relationship between the exposure level to wheat and fungal alpha-amylase and the development of sensitization and work-related respiratory symptoms. The demonstration of dose-response relationships is of importance in determining permissible concentrations for prevention.⁷⁴ However, there are

uncertainties with respect to the relative importance of peak versus average levels of exposure, the risk of sensitization at low concentrations (i.e., the 'no-effect level'), and the shape of the dose-response curve.

Studies investigating the shape of the relationship between flour dust exposure and wheat allergen levels suggest that the dose-response relationship for sensitisation may be non-linear and may even level off or decline at higher exposure levels.^{60,75,76} There have been no clear indications of an exposure level below which the risk for sensitization is zero or negligible.

2.7 HOST-ASSOCIATED RISK FACTORS FOR ALLERGIC SENSITISATION AND ASTHMA ASSOCIATED WITH FLOUR DUST

Various studies have reported that only a small proportion of workers develop occupational asthma (OA), although these workers have similar workplace exposures. This suggests that potential underlying differences in individual susceptibility due to host specific factors are also important considerations. The host factors that have been incriminated in the development of OA, are outlined below.

Genetics

Developments in human genetics in the past decade have also directed research towards investigating the genetic basis of individual susceptibility to OA development. Several genetic studies have demonstrated an association between certain human leucocyte antigen (HLA) class II molecules and single nucleotide polymorphisms (SNPs) with occupational asthma caused by various agents (isocyanates, red cedar, acid anhydrides, platinum salts, natural rubber latex, laboratory animals).⁷⁷ Recent Korean studies have

suggested that genetic factors may also be important in the development of work-related respiratory symptoms and sensitization to wheat flour in bakery workers. Cho et al⁷⁸ found that Toll-like receptor 4 (TLR4) gene polymorphisms are associated with allergic sensitization to wheat flour. While Hur et al⁷⁹ reported that genetic polymorphisms of β 2-adrenergic receptors (ADRB2) may contribute to the development of work-related symptoms in workers exposed to wheat flour, leading to baker's asthma.

Atopy

Atopy, has been defined as an increased propensity to produce an IgE antibody response to low-dose environmental aeroallergens, and can be established by assessing the presence of IgE antibodies against common inhalant allergens.⁷⁷ It is estimated that 20 to 35% of the population are affected by atopy associated with allergic disease, with about 60% of asthmatics being atopic.⁸⁰ Studies investigating occupational asthma among bakers have reported a positive correlation between atopy and the development of sensitisation and asthma.^{81,82} A recent study among bakers and pastry makers, also reported atopy as being an independent risk factor for occupational asthma.⁸³ Results from exposure-response studies suggest that atopy is an important modifier of sensitisation in bakery workers, as evidenced by having a more pronounced exposure-response relationship compared to non-atopic bakers.⁶⁰

Age

The effect of age on the development of asthma has been inconsistent. Studies of new-onset asthma among adults suggests that the risk decreases with advancing age.^{84,85} However, advancing age has been shown to increase the risk of occupational asthma among farmers.⁸⁶ A review on occupational allergy and asthma among bakery workers, suggests that age

does not appear to be associated with sensitisation or work-related respiratory symptoms.¹⁴

Gender

Gender has not been shown to be associated with sensitisation or work-related symptoms among bakery workers.¹⁴ It has been postulated that the increased risk of occupational asthma associated with gender can be ascribed to the gendered distribution of work.⁷⁷ This has been shown in studies of asthma and occupational exposures to cleaning agents, which clearly demonstrate an increased risk among females since they are more likely to be exposed to various cleaning agents than men.⁸⁷

Smoking

Smoking has been shown in some studies to increase the risk of sensitisation in bakery workers exposed to flour.^{16,88} However, whilst one study showed an increased risk of sensitisation in bakery workers¹⁶, others have demonstrated that smoking does not appear to increase the risk of asthma.^{15,60} It can be regarded as an inconsistent risk factor for baker's allergy and asthma.

2.8 PREVENTION STRATEGIES FOR REDUCING FLOUR DUST EXPOSURE AND BAKER'S ASTHMA

Exposure-response relationships studies for wheat allergen exposure suggest that reducing the exposure to flour dust allergens is likely to reduce the burden of allergic respiratory disease. Results from various studies demonstrate evidence of a direct relationship between occupational asthma and exposure to airborne allergens.⁷² Furthermore, these studies have

shown that the intensity of exposure to sensitizing agents is the most important risk factor for occupational asthma. Primary prevention strategies aimed at reducing workplace exposure to sensitizing agents would be the most rational approach for reducing the burden of occupational asthma.⁸⁹ The exposure-response relationships studies for wheat allergen exposure described earlier suggest that reduction of allergen exposure levels may reduce the number of sensitized bakery workers.⁶⁰ However, despite the overwhelming evidence that workplace exposures to flour dust should be controlled, prevention strategies in bakeries appear to have not been very satisfactory. While various countries have proposed exposure limits for flour dust, some are not totally protective and minimal action beyond general requirements has been applied.⁹⁰

a) Regulatory exposure standards

In December 2001, the Regulations for Hazardous Biological Agents were promulgated in South Africa under the Occupational Health and Safety Act. This regulation required that risk assessments be performed as well as regular industrial hygiene monitoring and medical surveillance be conducted using sensitive and effective procedures.⁹¹ However, the primary focus of this regulation has been on preventing and controlling microbial infections. The lack of emphasis on protein allergens causing allergic disease in the absence of microbial infections in these Regulations suggests the need for the development of specific South African regulations that deal with allergens of biological (protein) origin.⁹²

In the absence of specific regulatory exposure standards for allergens of biological origin in South Africa, the only other standard of relevance are the Regulations for Hazardous Chemical Substances (HCS) also promulgated under the Occupational Health and Safety Act (OHSA). These regulations require regular environmental monitoring and medical surveillance of workers at high risk of developing adverse health effects associated with exposure to

respiratory sensitisers.^{93,94} Under these regulations grain dust is defined as "dust arising from harvesting, drying, handling, storage or processing of barley, wheat, oats, maize, rye, including contaminants". Grain dust has been designated an exposure control limit of 10 mg/m³ TWA (total inhalable dust) and is denoted as a sensitizer (exposure should be prevented especially activities giving rise to short-term peak concentrations). In addition to this standard being much higher than international standards it is not directly applicable to bakery workers since the allergenicity of unmilled grain is different compared to milled grain to produce flour and is therefore not appropriate for bakeries.

The high sensitisation potential of flour dust makes the South African grain standard inadequate in protecting the health of bakery workers. Cullinan et al¹⁵ showed strong relationships between exposure to flour dust and health endpoints such as sensitisation and various work-related symptoms. These endpoints were observed at flour dust levels well below 10 mg/m³. Should the exposure levels not be considerably reduced to below 10 mg/m³ MEL (maximum exposure limit) as is currently the practice in South African bakeries, sensitisation, work-related respiratory symptoms, asthma and rhinitis are still likely to occur, based on the epidemiologic evidence.⁹⁵ This points to the need for specific exposure limits aimed at flour dust allergens such as wheat, rye and α -amylase in South Africa.

Unlike South Africa, the American Conference of Government Industrial Hygienists (ACGIH) have adopted a threshold limit value (TLV) of 0.5 mg/m³ and in Holland the Dutch Expert Committee of the Health Council had adopted a grain dust limit of 1.5mg/m³.^{95,96,97}

b) Workplace interventions

Prevention of occupational asthma related to a work-sensitizing agent, is best achieved at the workplace through primary prevention measures such as avoidance, or reduction of the occupational exposures.⁹⁸ Exposure reduction is crucial as it is estimated that approximately one third of workers with occupational asthma are unemployed up to six years after diagnosis.^{99,100} There is evidence suggesting that reduction in exposure leads to reduction in disease burden.^{101, 102} While there have been some notable successes in reducing occupational asthma especially from latex in health care workers,¹⁰³ several studies however indicate that there has been no decrease in exposure to flour dust allergens in the last decade.^{104,105} Several dose-response studies indicate that in some cases exposure levels will need to be reduced 10-fold or more to have a significant impact on sensitisation and respiratory health effects associated with flour and enzymes.^{21,60}

While total avoidance is not possible in bakeries, exposure reduction is the preferred approach. However, there are a few well-designed systematic intervention studies with detailed exposure characterisation data to determine the effect of exposure reduction in the occupational exposure levels. In addition little is known about the changes in incidence and prevalence of occupational asthma over time.¹⁰⁶ Studies that describe the effectiveness of control measures specifically in bakeries are few. Since only a limited number of exposure reduction measures have been studied in practice, little is therefore known about the effectiveness and efficacy of many exposure reduction measures.¹⁰⁷

Recently, some new data is emerging on the effectiveness of various interventions and control measures in bakeries.^{56,108} Although the data demonstrate varying degrees of effectiveness these studies do provide

insight into their potential to reduce exposure in bakeries.¹⁰¹ It has been demonstrated that local ventilation concentrated to flour release points, such as weighing stations, dough making machines, dough brakes, and bread machines, can reduce dust exposures to concentrations below 1 mg/m³.¹² A large scale Dutch study showed that control measures that were introduced during weighing of ingredients, especially by limiting the use of bagged flour products and the enclosure of silo's (when dumping flour), significantly decreases exposure.¹⁰⁸ While, other investigators have suggested that automation of parts of the process is a long-term option that can lead to considerably lower levels of exposure.¹⁰⁹

A systematic review (2012) on the effectiveness of general occupational health and safety (OHS) *training* confirms that such training promotes safer work practices among workers and recommends that workplaces continue to deliver OHS training as part of a larger risk management program. It cautions however that training alone will not necessarily prevent injuries and illnesses.¹¹⁰ Fishwick and colleagues also demonstrated the relevance of *education* in reducing workers' exposures.¹¹¹ In this study a significant excess of work-related symptoms and work-related specific IgE was observed in those who received no training (12% versus 1%, $p < 0.001$).¹¹¹ A sector-wide intervention programme in Dutch bakeries aimed primarily at education of workers showed a rather limited effect on exposure levels.¹⁰⁵ The authors concluded that although workers' knowledge on the risk of flour dust exposure improved, the change in work practices was rather limited. Overall, this information suggests that the use of appropriate knowledge and effective flour dust control measures, coupled with training and supervision, has the potential to reduce flour dust exposures in bakeries.

Very few studies have demonstrated the effectiveness of *personal protective equipment* in respect of reducing exposure to high allergen loads in general and flour dust in particular. The use of respiratory protective equipment can only offer protection when it is worn properly, removed safely and either

replaced or maintained regularly. A recent review on the primary prevention of occupational asthma reported several examples of indirect evidence that use of respiratory protective devices may prevent asthma onset, by demonstrating that respirators can reduce exposures to agents that can cause occupational asthma.¹⁰⁷

Certain *work practices* to avoid flour dust becoming airborne have also been suggested such as careful bag emptying and bag handling, and the use of vacuums instead of pressurised air for cleaning activities. During the dough making process, a major source of wheat exposure occurs when dough is covered with flour, to prevent sticking to work surfaces. It has been shown that for specific products a *change in work practice* such as the use of divider oil could reduce exposures. Studies by Burstyn et al^{112,113} demonstrated a 28-fold decrease in flour dust exposure when substituting dusting flour with divider oil, whilst Meijster et al¹⁰⁸ reported a rather modest reduction in exposure when substitutes like divider oil and dust-free flour were used.

The first case study report on flour dust and occupational asthma among two patients concluded that dust respirators were effective in preventing asthmatic reactions induced by buckwheat and wheat flour.¹¹⁴ In a later study on wheat allergen exposure investigators compared exposure levels measured inside a P2 particle filter facemask with measurements taken outside the facemask. In this study, the authors demonstrated that exposures were reduced by 93–96% using these facemasks, and concluded that these respirators may help to prevent baker's asthma.¹¹⁵ Nevertheless many studies have shown the personal protective equipment, although in cases very effective, is especially vulnerable to wrongly and ineffective use and should thus only be used as a last resort for exposure reductions in cases where all other options are not possible.

c) Surveillance

i) Environmental exposure level monitoring

Environmental exposures need to be adequately monitored to assess effectiveness of interventions. Monitoring of dust as opposed to allergen levels has its limitations in that dust levels may only partially correlate with the actual allergen concentrations. Furthermore, as has been suggested it is questionable whether dust levels are a valid exposure parameter in occupations where IgE-mediated allergies predominate. Studies show that the correlation between concentrations of dust and wheat allergen is moderate, but poor for fungal α -amylase.¹³

ii) Medical surveillance

Medical surveillance is a form of secondary prevention through a process of early detection of a disease (ie. sensitisation as an early marker for developing allergic respiratory disease) among workers before the development of severe adverse health effects (ie. work-related symptoms and/or baker's asthma).¹² Medical surveillance aims to detect occupational asthma in workers at an early stage and to remove those sensitized before the allergic respiratory disease becomes severe or irreversible.¹¹⁶ The most widely used method for medical screening and surveillance of occupational allergic respiratory disease are questionnaires, immunological test and spirometry.⁹⁸ The use of skin prick test and specific IgE for workers exposed to flour allergens has been shown to have a high predictive value in individuals who have subsequently developed asthma.¹¹⁶

However, the effectiveness of medical surveillance in the baking industry (or in any other field of occupational asthma) has not been systematically evaluated. A study by Gordon et al¹¹⁷ among bakery workers showed that workers who reported respiratory symptoms in a screening questionnaire

were no more likely to have asthma (or occupational asthma) than those who responded negatively. Furthermore, a study among supermarket bakery workers that compared an independent cross-sectional survey with a routine in-house company surveillance programme suggested that health surveillance can underestimate the burden of occupational asthma by a factor of 4-7.¹¹⁸

A recent review on the benefits of medical screening, reported on new approaches to medical surveillance that are based on developing diagnostic models to enable the prediction of the probability of sensitisation in workers exposed to high molecular weight allergens.¹¹⁹ These models use questionnaire-based predictions that enable risk stratification of workers and allows for identifying workers requiring further clinical evaluation. Two studies among bakery workers have demonstrated that simple short questionnaires, developed to predict flour sensitisation can accurately identify those at risk of developing work-related allergic respiratory disease.^{120,121}

In *conclusion*, it is evident that despite the high prevalence of baker's allergy and asthma in certain high risk working populations, further research needs to focus on characterising the specific asthma phenotypes and their prevalence in bakery workers. While baker's allergy and asthma is well described, investigations into the extent to which occupational exposure to various allergens constituted a risk to the health of bakery workers in supermarkets are limited. The shift in location of bakery production and innovations in the baking industry implies that the distribution and determinants of baker's asthma will inevitably also change. It is therefore important that these changes are investigated and monitored in order to anticipate and prevent baker's asthma in the future.

Characterizing the complex interactions between environmental factors and individual susceptibility is a crucial step in identifying the factors that determine the development of baker's allergy and asthma. Environmental

determination of bakery allergens is an essential aspect of demonstrating exposure-response relationships. Therefore studies primarily aimed at evaluating exposure also need to employ standardized methodologies to allow for a robust quantification and characterization of allergens and for comparisons across populations at risk of developing baker's allergy and asthma. While the nature of exposure response relationships has been investigated to some extent, the clinical endpoints have focussed primarily on allergic sensitisation and work-related symptoms, rather than baker's asthma, which is the most disabling of outcomes. Further exploration is also needed of factors that attenuate or enhance exposure-response relationships such as host susceptibility, other environmental co-factors, such as endotoxins and chemical pollutants, gene-environment interactions and the role of other pathophysiological mechanisms that may underlie these responses.

Finally, to arrive at an accurate estimate of the impact of interventions, studies are needed that allow for the detailed evaluation of the impact of specific interventions if implemented on their own or in a multi-faceted manner to reduce the exposure to flour dust in those at risk. Future studies also need to evaluate the long term and sustained impact of exposure reductions on reducing associated allergic respiratory disease among bakery workers, which may best be achieved best through cohort studies.

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CHAPTER 3

DETERMINANTS OF ASTHMA PHENOTYPES AMONG SUPERMARKET BAKERY WORKERS.

University of Cape Town

CHAPTER 3

Determinants of asthma phenotypes among supermarket bakery workers.

Paper overview

This paper documents the baseline health assessment results for the study population. It describes the prevalence and determinants of different asthma phenotypes in supermarket bakery workers.

Contribution to the thesis and novelty

This article addresses the first objective of the research and describes the various asthma phenotypes in supermarket bakery workers in relation to host risk factors and self-reported exposure to flour dust. While baker's asthma has been well described, various asthma phenotypes in bakery workers have not been comprehensively characterized.

Role of candidate

The candidate was a key member of the research team; developed the protocol under guidance of Prof Jeebhay in relation to the very technical medical aspects, designed the questionnaires and all other data collection instruments. The candidate was involved in the data collection process, data management, quality control of the fieldwork and solely conducted all the data analysis. The candidate wrote the manuscript, incorporated input from collaborators who critically reviewed the manuscript, and submitted the final manuscript.

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Appendices related to this paper

Appendix 2: Informed consent

Appendix 3: Questionnaire

Appendix 4: Skin prick test (pre-test & data collection sheet)

Appendix 5: Lung function test (pre-test & data collection sheet)

University of Cape Town



Determinants of asthma phenotypes in supermarket bakery workers

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ABSTRACT: While baker's asthma has been well described, various asthma phenotypes in bakery workers have yet to be characterised. Our study aims to describe the asthma phenotypes in supermarket bakery workers in relation to host risk factors and self-reported exposure to flour dust.

A cross-sectional study of 517 supermarket bakery workers in 31 bakeries used a questionnaire, skin prick tests, and specific immunoglobulin E to wheat, rye and fungal α -amylase and methacholine challenge testing.

The prevalence of probable occupational asthma (OA, 13%) was higher than atopic (6%), nonatopic (6%) and work-aggravated asthma (WAA, 3%) phenotypes. Previous episodes of high exposure to dusts, fumes and vapours causing asthma symptoms were more strongly associated with WAA (OR 5.8, 95% CI 1.7–19.2) than OA (2.8, 1.4–5.5). Work-related ocular–nasal symptoms were significantly associated with WAA (4.3, 1.3–13.8) and OA (3.1, 1.8–5.5). Bakers with OA had an increased odds ratio of reporting adverse reactions to ingested grain products (6.4, 2.0–19.8).

OA is the most common phenotype among supermarket bakery workers. Analysis of risk factors contributes to defining clinical phenotypes, which will guide ongoing medical surveillance and clinical management of bakery workers.

KEYWORDS: Asthma phenotypes, bakery workers, determinants, risk factors, work-related asthma

It is well documented that exposure to flour dust increases the risk of respiratory diseases, particularly occupational asthma (OA). Studies conducted among bakery workers have reported the prevalence of baker's asthma to be 5–17% [1]. Asthma is commonly due to sensitisation to wheat, rye and fungal α -amylase allergens present in flour.

Asthma is generally not considered to be a single disease but rather a syndrome comprising a common set of symptoms. Different phenotypes of asthma are distinguished by variations in clinical features, trigger factors and differences in immunological and pathophysiological characteristics [2]. Age of onset, high numbers of eosinophils in the airways, atopic status, family history of asthma, early exposure to allergens and exposure to inhalation accidents (exposure to high levels of vapours, gas, dust or fumes) are important predictors of adult asthma phenotypes [2, 3]. While baker's asthma has been well described in various workplaces, phenotypes of asthma among bakery workers in a common workplace setting have yet to be characterised.

An evaluation of employment patterns in the baking industry worldwide over the past decade

has demonstrated a significant rise in franchise (in-store) bakeries [4]. In South Africa, in-franchise employment has risen from 20% of all employment in the baking industry in 1995 to 44% in 2002 [5]. This shift has increased the potential for workers to develop baker's allergy and asthma.

The aim of our study is to describe various asthma phenotypes observed in supermarket bakery workers of a large chain store in relation to host risk factors and self-reported exposures to flour dust.

Our study is part of a larger prospective intervention study aimed at reducing sensitisation to flour dust allergens in supermarket bakers. A detailed baseline environmental exposure assessment study was also conducted and is the subject of a separate communication.

MATERIALS AND METHODS

Study design, population and sampling

A cross-sectional study was conducted on 517 workers currently employed in all 31 bakeries belonging to a supermarket chain store in the Western Cape province of South Africa during

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the period June 2003 to June 2004. All permanent (n=318) and casual workers (n=168) in the bakery and ex-bakers with asthma moved from the bakery section 2 yrs prior to our study (n=31) were investigated. The protocol was approved by the University of Cape Town (Cape Town, South Africa) and the Institutional Review Board of the University of Michigan (Ann Arbor, MI, USA) prior to the study being conducted.

Questionnaire

Each worker completed the standard European Community Respiratory Health Survey (ECRHS) questionnaire [6] designed for the investigation of asthma. Additional questions relating to current and previous employment and degrees of exposure to flour dust and tobacco smoke were included. Smoking status was classified into the following three categories: never-smoker (lifelong abstinence), ex-smoker (defined as having quit completely >1 month prior to the survey) and current smoker. Self-reported high exposures were ascertained based on a positive response to the question: "Has there ever been an instance when you inhaled a large amount of vapour, gas, dust or fumes in any of these jobs that resulted in you developing a tight chest, wheeze or cough?". Also included were questions on domestic flour dust exposures and, in particular, the practice and frequency of baking activities in the home. For the purposes of our study, ocular–nasal symptoms were defined as a positive response to the question: "Have you ever had any nose or eye problems or allergies such as hay fever?". Upper and lower airway symptoms were considered to be work-related if they were reported to worsen during the work shift and improve when away from work. Ingestion-related adverse reactions were assessed based on responses to the question: "Have you changed your diet or avoided certain grain products (e.g. wheat/rye/soya) because they do not agree with you when you eat them?".

Immunological tests

Skin prick tests

Skin prick tests (SPTs) were performed using the following standard common local aeroallergens (ALK-Abelló A/S, Horsholm, Denmark): house dust mite (*Dermatophagoides pteronyssinus*), bermuda grass (*Cynodon dactylon*), rye grass (*Lolium perenne*), grass mix (Pollen III: Avena, Hordeum, Triticum, Secale), cockroach (*Blattella germanica*), cat (*Felis domesticus*), dog (*Canis familiaris*), mould mix (*Cladosporium herbarum*, *Alternaria alternata*, *Fusarium*) and *Aspergillus* (*Aspergillus fumigatus*). Commercially available SPTs of flours (wheat, rye, oat grain and barley grain) (Bencard, Neuss, Germany), soya and corn flour (Leti Alergia, Madrid, Spain), peanut and storage mite (*Lepidoglyphus destructor*), and fungal α -amylase (ALK-Abelló) were also used. For the analysis of correlations between various allergens, SPT reactivity was expressed as the allergen histamine wheal ratio, i.e. the mean wheal diameter at the allergen site divided by the mean wheal diameter at the histamine site [7]. A positive SPT was regarded as a wheal read 15 min after testing that had a diameter (mean of two perpendicular measures) of ≥ 3 mm more than the negative control. Areas of wheal were traced on clear tape and stored for later measurement. For the purposes of our study, atopy was considered to be present if the SPT to one or more common aeroallergens was positive.

Serum-specific immunoglobulin E

Serum-specific immunoglobulin (Ig) E levels were measured in 513 workers. The presence of atopy in workers who did not undergo SPTs (n=10) was defined by a positive Phadiatop® test (ImmunoCAP 100 System; Phadia, Uppsala, Sweden). Quantification of specific IgE antibodies to wheat (f4), rye (f5) and fungal α -amylase (k87) was performed using CAP-FEIA (fluorescence enzyme immunoassay) according to the manufacturer's instructions (Phadia). An ImmunoCAP result of >0.35 kU·L⁻¹ was regarded as positive.

Spirometry

Spirometry was performed using the Jaeger Aerosol Provocation System (APS) Pro apparatus according to American Thoracic Society guidelines [8]. Workers were required to refrain from smoking for 1 h, from using short-acting β_2 -agonist bronchodilators for 4 h, and from using oral asthma medications for 8 h prior to lung function testing. None were on long-acting bronchodilators. Pulmonary function reference values of the European Community for Coal and Steel with lower limits corresponding to the 95th percentile were used where appropriate, and the locally derived reference equation for South African university workers was applied [9, 10].

Methacholine challenge testing

Methacholine challenge testing was performed on all workers by trained technologists according to an abbreviated protocol used in epidemiological surveys. The Medic Aid Pro Nebulizer dosimeter method involved a protocol of increasing numbers of breaths to achieve pre-defined cumulative doses of methacholine [11]. The doses were delivered by the Jaeger APS MedicAid Side Stream APS-Nebulizer (Sensormedics, CA, USA) according to the manufacturer's instructions, commencing with the lowest dose of 0.026 mg. The dose was increased to a maximum dose of 2.048 mg methacholine (the provocative dose of methacholine causing a $\geq 20\%$ fall in forced expiratory volume in 1 s (FEV₁); PD₂₀ methacholine) if a positive end-point was not obtained. The results of the methacholine challenge test were interpreted as follows: borderline = 0.4 mg < PD₂₀ methacholine < 1.0 mg; mild = 0.08 mg > PD₂₀ methacholine < 0.4 mg; moderate/severe = PD₂₀ methacholine < 0.08 mg. Borderline values for PD₂₀ methacholine were considered negative in the definition of nonspecific bronchial hyperresponsiveness (NSBH). These cut-offs for the APS system were based on the results from a validation study performed on 40 hyperresponsive bakery workers. This study confirmed a satisfactory correlation between the APS cumulative PD₂₀ methacholine method and the standard VMAX (Sensormedics) method [11].

In subjects in whom PD₂₀ methacholine was contraindicated, such as those with acute asthma symptoms or a baseline FEV₁ <1.5 L or FEV₁ <70% predicted, a bronchodilator (400 μ g salbutamol dose) was administered instead. A change in FEV₁ of $\geq 12\%$ pred 10 min after administration of bronchodilator was considered suggestive of NSBH.

Among the 503 subjects who underwent normal spirometry, 422 performed interpretable PD₂₀ methacholine results. Two subjects were unable to produce reproducible FEV₁ manoeuvres, 38 subjects underwent bronchodilator challenge (post-bronchodilator), since PD₂₀ methacholine was contraindicated,

and 43 subjects had $\geq 10\%$ decrease in FEV₁ after administration of saline diluent, and were therefore not considered for PD₂₀ methacholine. The PD₂₀ methacholine was discontinued in three subjects; one requested the test to be stopped, and in two subjects the test was stopped because of technical problems.

Operational definitions of asthma phenotypes

Atopic asthma (AA) was defined as either having an asthma attack or use of asthma medication in the past 12 months or presence of NSBH, the presence of atopy, and the absence of sensitisation to bakery dust allergens [3].

Nonatopic asthma (NAA) was defined as either having an asthma attack or use of asthma medication in the past 12 months or the presence of NSBH, being nonatopic, and the absence of sensitisation to bakery dust allergens.

Work-aggravated asthma (WAA) was defined as either having an asthma attack or use of asthma medication in the past 12 months or the presence of NSBH, work-related chest symptoms, and the absence of sensitisation to bakery dust allergens.

Probable occupational asthma was defined as either having an asthma attack or use of asthma medication in the past 12 months or the presence of NSBH, and sensitisation to bakery dust allergens [12].

Sensitivity to bakery dust allergens was defined as either a positive SPT to any cereal allergen (wheat, rye, oats, barley, soya or corn) or elevated serum IgE to wheat, rye or α -amylase.

Statistical analysis

Statistical analysis was performed using STATA version 8 (StataCorp, College Station, TX, USA). Both continuous and categorical analyses were conducted. Key associations of interest were the relationships between host factor attributes (e.g. age, sex, smoking, past medical history, ingestion-related reactions to grain products and adult-onset asthma), and self-reported occupational exposures with asthma phenotypes. Multivariate logistic regression models adjusted for age, sex and smoking were used to determine the relationship between individual asthma phenotypes and predictor variables.

RESULTS

Study population

A total of 517 workers from all 31 stores participated in our study. The demographic characteristics of the study population are outlined in table 1. Almost half the participants (47%) were current smokers, with an average of 5 pack-yrs smoking history. Of the currently employed workers, 41% were bakers or assistant bakers, 27% counterhands and 10% confectioners. Among the workers with self-reported adverse reactions to grain products, a larger proportion (63%) attributed this to rye products.

Immunological characteristics

The prevalence of sensitisation to common inhalants were as follows: house dust mite (*D. pteronyssinus*), 33%; rye grass (*L. perenne*), 20%; grass mix (*Pollen III*), 18%; cockroach (*B. germanica*), 11%; bermuda grass (*C. dactylon*), 10%; dog (*C. familiaris*), 8%; mould mix (*Cladosporium*, *A. alternate*, *Fusarium*), 7%; cat

(*F. domesticus*), 4%; and aspergillus (*A. fumigatus*), 3%. The overall prevalence of atopy, defined as a positive SPT to one or more common aeroallergens, was 42%, while 12% were positive to more than three aeroallergens. The prevalence of sensitisation to any of the bakery dust allergens was 33% (table 2). The most common sensitisers on SPT were cereal flours wheat (16%) and rye (16%). However, higher proportions of workers (26 and 24% to wheat and rye flours, respectively) had elevated IgE levels to flours, but the prevalence of elevated IgE to α -amylase remained low (4%). A high degree of correlation was found for subjects sensitised to a number of the various cereal flours, especially wheat, rye, barley and corn flour (Spearman's $r=0.67$ – 0.75 , $p<0.001$). Comparison of wheat SPT *versus* wheat IgE, as well as rye SPT *versus* rye IgE, showed a high degree of correlation (Spearman's $r=0.71$ – 0.73 , $p<0.0001$) between these two indices of allergic sensitisation with the kappa statistic demonstrating

TABLE 1 Demographic characteristics of supermarket bakery workers

Demographic characteristics

Subjects n	517
Age yrs	32 \pm 9
Sex F:M	51:49
Smoking status	
Current smokers	47
Ex-smokers	10
Never-smokers	43
History of current smokers pack-yrs	5
Occupation	
Baker/assistant baker	41
Counterhand	27
Confectioner	10
Manager	6
Supervisor	6
Ex-baker [#]	6
General worker	3
Cleaner	1
Duration of employment in bakery yrs	6 \pm 5
Duration of employment in current job yrs	4 \pm 4
Past history of lung disease (self-reported)	
Repeated childhood chest infections	5
Previous treatment for tuberculosis	7
Previous treatment for chronic bronchitis	5
Family history of atopy[*]	54
Self-reported adverse reactions to grain products⁺	3
Rye products	63 [§]
Whole-wheat products	19 [§]
White bread	12 [§]
Breakfast cereals	6 [§]
Baking activities at home	38
Training received on health risks of flour dust	8

Data are presented as % or mean \pm SD, unless otherwise indicated. F: female; M: male. [#]: removed from the bakery in the last 2 yrs due to baker's asthma; ^{*}: defined as positive answer to the question "Does any member of your family (blood relatives) have any kind of allergies (e.g. hay fever, eczema, asthma)?"
⁺: n=16; [§]: as a proportion of the sub-group (n=16).

TABLE 2 Allergic sensitisation profiles for potential occupational allergens among supermarket bakery workers

Occupational allergen	Allergic sensitisation profiles		
	Overall	Atopic	Nonatopic
Total subjects	507	213	294
Skin prick test[#]			
Wheat flour	79 (16)	52 (24)	27 (9)
Rye flour	82 (16)	55 (26)	27 (9)
Corn flour	73 (14)	51 (24)	22 (7)
Barley	59 (12)	40 (19)	19 (6)
Soya	42 (8)	32 (15)	10 (3)
Oats	41 (8)	31 (15)	10 (3)
Storage mite (<i>Lepidoglyphus destructor</i>)	73 (14)	67 (31)	6 (2)
Peanut	30 (6)	28 (13)	2 (1)
Fungal α -amylase	17 (3)	13 (6)	4 (1)
Specific IgE^{†,‡}			
Wheat flour	134 (26)	90 (42)	44 (15)
Rye flour	123 (24)	81 (38)	42 (14)
Fungal α -amylase	21 (4)	15 (7)	6 (2)
At least one bakery dust allergen (any cereal or amylase)[§]	172 (33)	113 (52)	59 (20)

Data are presented as n and n (%). Each result represents sensitisation to an individual allergen, with some workers sensitised to more than one allergen. Ig: immunoglobulin. [#]: test carried out on 507 subjects; [†]: test carried out on 513 subjects; [‡]: serum-specific IgE >0.35 kU·L⁻¹; [§]: positive on skin prick test and/or elevated IgE. Note: Chi-squared test between atopic versus nonatopics significant (p<0.0001) for all allergens, except for fungal α -amylase (p<0.01).

moderate to substantial agreement (kappa=0.55–0.64) between the tests. Workers sensitised to more than three aeroallergens were more likely to be sensitised to occupational allergens (OR 9.5, 95% CI 4.9–18.2).

Respiratory symptoms

The prevalence of work-related ocular–nasal symptoms (31%) was higher than work-related chest symptoms (17%; table 3). Over half the workers with doctor-diagnosed asthma (13%) reported adult-onset asthma, and 38% of these reported current ocular–nasal symptoms. 30 (6%) workers reported job changes prompted by work-related chest symptoms. Of these, 14 had worked as bakers/assistant bakers, 10 as counterhands, four as confectioners and two as a supervisor/controller prior to being relocated. A significantly higher proportion of females had shortness of breath (10%), current asthma treatment or attacks (9%), but a lower proportion (8%) reported symptoms associated with episodes of high exposure to flour dust. An evaluation of the sensitivity and specificity of the questionnaire to predict asthma and, more specifically, OA revealed that work-related chest symptoms were highly specific (89%) for both outcomes, but were not very sensitive (31–43%) in accurately predicting the presence of NSBH and OA, respectively.

Pulmonary function and NSBH

The results of pulmonary function and nonspecific bronchial challenge tests are presented in table 4. Using European Community of Coal and Steel reference values, 17% of workers had an FEV₁ of <80% pred, while only 7% had evidence of airflow obstruction defined as a pre-bronchodilator FEV₁/forced vital capacity (FVC) ratio of <0.70. Using an alternative set of

reference values according to WHITE *et al.* [10], the prevalence of FEV₁ <80% pred was 9%. A total of 22% of workers had evidence of bronchial hyperresponsiveness (19% positive on the methacholine challenge test (PD₂₀ methacholine <0.4 mg)), and 3% positive on the basis of an increase in FEV₁ of ≥12% after

TABLE 3 Upper and lower respiratory symptoms among supermarket bakery workers

Symptom	Prevalence
Subjects n	517
Asthma history	
Doctor-diagnosed asthma	67 (13)
<17 yrs	30 (6)
≥17 yrs	37 (7)
Current use of asthma medication	36 (7)
Asthma attack in the past year	31 (6)
Work-related asthma symptoms	
Episode of high exposure causing tight chest, wheeze or cough	67 (13)
Work-related chest symptoms	86 (17)
Job change due to work-related chest symptoms	30 (6)
Upper airway symptoms	
Ocular–nasal symptoms	196 (38)
Work-related ocular–nasal symptoms	162 (31)

Data are presented as n (%), unless otherwise indicated.

bronchodilator), with a further 10% having “borderline” results (PD₂₀ methacholine ≥ 0.4 mg and <1.0 mg).

Correlation between lung function and wheat and rye-specific IgE

There was a significant negative correlation between PD₂₀ methacholine and IgE levels with wheat (Spearman $r = -0.30$, $p < 0.001$) and rye (Spearman $r = -0.28$, $p < 0.001$) flour. Stratifying the IgE data by atopic status revealed similar inverse relationships between PD₂₀ methacholine and IgE among atopics (Spearman $r = -0.26$, $p < 0.001$) and nonatopics (Spearman $r = -0.21$, $p < 0.001$) for wheat and rye. The degree of airway obstruction on baseline spirometry (FEV₁/FVC) was also inversely correlated with wheat IgE (Spearman $r = -0.15$, $p = 0.001$). However, no correlation was observed between FEV₁ and wheat-specific IgE (Spearman $r = -0.07$, $p = 0.090$). Similar patterns of association were observed for rye flour (data not shown).

Asthma phenotypes in relation to risk factors

Among the asthma phenotypes described, the prevalence of probable OA (13%) was much higher than AA (6%), NAA (6%) and WAA (3%) phenotypes (table 5). A large proportion (55 (92%) out of 60) of workers with OA had NSBH, whilst only 55 (12%) workers showed evidence of occupational rhinitis without asthma. In the multivariate logistic regression analysis, having recurrent chest infections as a child (OR 5.5) was significantly associated with WAA. Elevated odds ratios were demonstrated for the associations between atopy and OA, particularly in individuals with polysensitisation to common aeroallergens. Previous episodes of high exposure that caused asthma symptoms were associated more strongly with WAA (OR 5.8) than probable OA (OR 2.8). Those with OA were significantly more likely to be supervisors or managers

(OR 4.0) at the time of the study. There was a six-fold increased odds (OR 6.4) of self-reported ingestion-related adverse reactions to grain products in OA, and more so in the NAA subgroup. No association was found with baking at home and any of the asthma phenotypes. Using alternative definitions for probable OA, which included subjective work-related symptoms in this definition decreased the prevalence to 7%. However, the significant association with predictors of this phenotype persisted and demonstrated higher odds ratios for ocular–nasal symptoms (OR 13.0), previous episodes of high exposure causing asthma symptoms (OR 5.0), as well as self-reported ingestion-related adverse reactions to grain products (OR 13.3).

DISCUSSION

This study of supermarket bakeries provides a useful insight into the relative prevalence of and risk factors for different phenotypes of asthma among workers in this emerging and relatively poorly regulated industry. Asthma phenotypes were defined on the basis of clinical asthma, airway hyperresponsiveness, atopic status and sensitisation to occupational allergens. This study has demonstrated that the prevalence of probable OA (13%) in the industry is considerably higher than that of both AA (6%) and NAA (6%) and the WAA phenotype (3%). Furthermore, the overall prevalence of AA in this cohort is at the lower end of the spectrum of adult asthma reported in developed countries (8–12%), but higher than the national average reported for South Africa (4%) [13, 14]. The higher prevalence of asthma observed in this group may be attributed to these bakeries being located in a highly urbanised province (Western Cape), which has a higher population prevalence (8%) of adult asthma [15]. This study also demonstrated that 50% of the adult asthma phenotype is atopic, as has been reported in previous studies [16].

TABLE 4 Pulmonary function indices among supermarket bakery workers

Pulmonary function indices [#]	Overall	Males	Females	p-value
Subjects n	503	243	260	
FEV₁ L	3.16 \pm 0.77	3.63 \pm 0.71	2.72 \pm 0.52	
FVC L	3.83 \pm 0.88	4.45 \pm 0.71	3.25 \pm 0.57	
FEV₁ % pred	92 \pm 14	91 \pm 14	93 \pm 14	0.002 ⁺⁺
FVC % pred	95 \pm 13	94 \pm 12	97 \pm 13	0.055 ⁺⁺
FEV₁/FVC	83 \pm 9	81 \pm 10	84 \pm 8	0.019 ⁺⁺
FEV₁/FVC <70% n	33 (7)	20 (8)	13 (5)	0.144 ^{§§}
FEV₁ <80% pred n	84 (17)	42 (17)	42 (16)	0.107 ^{§§}
FEV₁ <80% pred[†] n	43 (9)	25 (10)	18 (7)	0.177 ^{§§}
Bronchial hyperresponsiveness n				
≥ 12% FEV ₁ increase post-bronchodilator ⁺	16 (3)	7 (3)	9 (3)	0.086 ^{§§}
≥ 10% FEV ₁ decrease post-saline diluent [‡]	43 (9)	18 (7)	25 (10)	0.269 ^{§§}
Methacholine challenge test PD ₂₀ methacholine <0.4 mg [‡]	94 (19)	37 (15)	57 (22)	0.012 ^{§§}
NSBH ^{##,††}	110 (22)	44 (18)	66 (25)	0.030 ^{§§}

Data are presented as mean \pm sd or n (%), unless otherwise indicated. FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; % pred: % predicted; PD₂₀ methacholine: provocative dose of methacholine causing a $\geq 20\%$ fall in FEV₁; NSBH: nonspecific bronchial hyperresponsiveness. [#]: pre-bronchodilator values, unless stated otherwise; [†]: using the locally derived reference equation for South African university workers; ⁺: 38 completed the test; [‡]: 465 completed the test; [§]: 419 completed the test; ^{##}: 457 completed the test; ^{††}: NSBH defined as any of the following two criteria: PD₂₀ methacholine <0.4 or $\geq 12\%$ increase in FEV₁ after administration of a bronchodilator; ⁺⁺: two-sample unpaired t-test; ^{§§}: Chi-squared test with one degree of freedom.

TABLE 5 Risk factors associated with asthma phenotypes among supermarket bakery workers in multivariate models

	AA	NAA	WAA	Probable OA	Probable OA	
					Atopic	Nonatopic
Prevalence	29 (6) [#]	29 (6) [#]	13 (3) [#]	60 (13) [#]	42 (22) [†]	18 (7) ⁺
Determinants						
Family history of asthma	1.53 (0.55–4.26)	0.76 (0.22–2.65)	1.91 (0.50–7.33)	1.06 (0.49–2.28)	0.95 (0.37–2.42)	0.95 (0.20–4.43)
Atopy			1.23 (0.41–3.76)	4.15 (2.29–7.53) ^{***}		
Polysensitisation (>3 aeroallergens)	6.28 (2.72–14.52) ^{***}		2.54 (0.65–9.93)	5.54 (2.78–11.03) ^{***}		
Past medical history						
Childhood onset (<17 yrs) asthma	2.20 (0.68–7.11)	1.81 (0.49–6.75)	2.75 (0.54–13.95)	2.13 (0.81–5.62)	2.08 (0.69–6.27)	
Pulmonary tuberculosis	0.57 (0.07–4.46)	2.06 (0.64–6.62)	4.07 (0.99–16.64)	1.92 (0.77–4.79)	2.90 (0.80–10.51)	1.53 (0.31–7.51)
Chronic bronchitis	1.81 (0.39–8.40)	2.59 (0.69–9.74)	4.47 (0.89–22.49)	2.01 (0.71–5.70)	1.94 (0.46–8.22)	2.44 (0.46–12.84)
Recurrent childhood chest infections	1.21 (0.27–5.55)	2.91 (0.89–9.53)	5.46 (1.02–29.17) [*]	0.81 (0.23–2.77)	2.27 (0.48–10.66)	
Upper airway symptoms						
Ocular–nasal symptoms	2.44 (1.12–5.29) [*]	0.51 (0.21–1.25)	2.91 (0.92–9.20)	6.02 (3.26–11.11) ^{***}	4.48 (1.97–10.23) ^{***}	7.11 (2.39–21.09) ^{***}
Work-related ocular–nasal symptoms	1.56 (0.72–3.39)	0.73 (0.30–1.78)	4.30 (1.34–13.77) [*]	3.13 (1.78–5.49) ^{***}	2.51 (1.21–5.19) [*]	3.53 (1.27–9.81) [*]
Age of first exposure to flour dust allergens	1.16 (1.01–1.33) [*]	0.99 (0.91–1.09)	1.01 (0.89–1.16)	1.00 (0.94–1.07)	0.99 (0.92–1.08)	1.00 (0.91–1.10)
21–30 yrs [§]	1.93 (0.70–5.31)	1.64 (0.56–4.82)	8.66 (0.97–77.28)	1.04 (0.51–2.12)	1.08 (0.45–2.62)	1.23 (0.28–5.42)
>30 yrs	3.09 (0.51–18.71)	1.72 (0.34–8.78)	1.30 (0.05–34.96)	0.65 (0.20–2.04)	0.46 (0.10–2.22)	0.99 (0.13–7.59)
Previous episodes of high exposure causing asthma symptoms	1.43 (0.51–4.00)	2.33 (0.87–6.22)	5.77 (1.74–19.15) ^{**}	2.80 (1.43–5.52) ^{**}	2.70 (1.07–6.83) [*]	3.61 (1.15–11.30) [*]
Current job status^f						
Baker	0.37 (0.11–1.18)	0.50 (0.17–1.46)	0.10 (0.01–1.18)	1.57 (0.66–3.74)	2.14 (0.78–5.88)	1.68 (0.14–20.77)
Confectioner	0.29 (0.05–1.74)	0.49 (0.09–2.65)	0.93 (0.11–8.20)	1.12 (0.27–4.60)	0.51 (0.06–4.56)	4.86 (0.30–78.05)
Supervisor/manager		0.39 (0.06–2.35)	0.34 (0.02–5.98)	4.01 (1.28–12.59) [*]	5.41 (1.26–23.15) [*]	7.48 (0.49–115.05)
Self-reported ingestion- related adverse reactions to grain products				6.35 (2.03–19.83) ^{**}	2.66 (0.56–12.65)	13.43 (2.23–80.83) ^{**}
Baking activities at home	0.53 (0.22–1.28)	0.46 (0.19–1.13)	0.73–0.22–2.44)	1.11 (0.63–1.94)	1.63 (0.79–3.34)	0.72 (0.26–2.02)

Data are presented as n (%) or OR (95% CI). AA: atopic asthma; NAA: nonatopic asthma; WAA: work-aggravated asthma; OA: occupational asthma. [#]: out of a total of 457; [†]: out of a total of 188; ⁺: out of a total of 269; [§]: age category ≤20 yrs used as reference category; ^f: counterhands used as reference group. *: p<0.05; **: p<0.01; ***: p<0.001. Each odds ratio is a separate regression model adjusted for age, sex and smoking status.

The prevalence of probable OA (13%) in our study is at the upper end of the range of prevalence data (5–13%) reported by studies in industrial bakeries in which a similar definition of OA (bronchial hyperresponsiveness and sensitivity to flour) was used [17, 18]. However, the prevalence was much higher than that reported among British supermarket bakery workers (4%), even after using an alternative definition that included work-related asthma symptoms (7%) [4]. The potential underestimation that could arise due to the healthy-worker effect was partially minimised in our study by the inclusion of ex-bakers in the study population. It should be noted that the inability to characterise the acute onset irritant-induced asthma phenotype in this study can be attributed to its low incidence in this setting as the production process in these bakeries mainly entails exposure to high molecular weight respiratory sensitisers in flour dust, although exposure to cleaning agents cannot be totally excluded [3].

In our study, a high proportion (22%) of bakery workers demonstrated NSBH. Females, had a significantly higher prevalence than males (25% *versus* 18%), which is consistent with previous studies in which females comprised the major proportion of study subjects [19]. Given that a greater proportion (62–94%) of males were employed in the more highly exposed jobs (*i.e.* baker, confectioner, manager) and females (98%) in the less-exposed jobs (*i.e.* counterhands), it is unlikely that the discrepancies observed are due to different job hiring practices for males and females. This distribution of work according to sex does not totally explain the different patterns of NSBH observed in our study, suggesting that other biological factors may play a role in the patterns observed [20].

It is well recognised that the most common flour dust allergens responsible for sensitisation in the OA phenotype among bakers

are cereal flours and synthetic enzymes [1]. This sensitisation pattern has also been observed in the current study, in which sensitisation to wheat, rye and other related cereal flours on SPT was high (16%), but less so for fungal enzyme α -amylase (4%). Preliminary data from the detailed exposure assessment study that was conducted confirmed that bakers had the highest average (geometric mean) wheat allergen concentration ($16.504 \mu\text{g}\cdot\text{m}^{-3}$), followed by confectioners ($7.307 \mu\text{g}\cdot\text{m}^{-3}$), whilst counterhands had the lowest exposures ($0.84 \mu\text{g}\cdot\text{m}^{-3}$). However, for most job titles, α -amylase concentrations were below the limit of detection ($1.083 \text{ ng}\cdot\text{m}^{-3}$). While sensitisation to cereal flours were highly correlated ($r=0.67\text{--}0.75$), a very high degree of correlation ($r=0.92$) was observed between wheat and rye. Interestingly, a large proportion (33%) of workers reported work-related asthma symptoms specifically to rye flour, despite this flour constituting a small proportion ($<10\%$) of products handled in these bakeries. It has been suggested that cross-reactivity between grain cereal allergens could be a possible mechanism for these observations [21]. Cross-reactivity between rye flour allergens and rye grass allergens remains another possibility, although this is unlikely as a very low correlation was observed between sensitisation to these allergens ($r=0.37$). While the response to rye may be immunologically mediated, the physical properties of rye flour may also produce an additional irritative effect, as demonstrated by its ability to produce a greater bronchial response compared with wheat [22].

In our study, a modest inverse correlation was demonstrated between PD₂₀ methacholine and specific IgE levels to wheat (Spearman $r=-0.30$; $p<0.001$) and rye flour (Spearman $r=-0.28$; $p<0.001$) that, as far as we can establish, has not been previously reported. However, there have been a few epidemiological studies among bakers that have reported an association between other markers of exposure (flour dust) and the degree of NSBH following nonspecific challenge tests using methacholine. PRICHARD *et al.* [23] reported that 41% of bakers *versus* 21% of controls (slicers/wrappers) had a positive methacholine challenge test (PD₂₀ methacholine $<30 \mu\text{mol}$). Similarly, MUSK *et al.* [24] showed the proportion of bakers with a positive methacholine challenge test in less exposed bakers increased from 26% to 42% in the more exposed group. BOHADANA *et al.* [25] reported a significant dose-response relationship with the duration of exposure to flour dust, while CHOUDAT *et al.* [26] demonstrated that flour dust exposure and smoking increase bronchial responsiveness, as measured by the slope of the dose-response curve to methacholine.

In our population, atopy was identified as an important contributor to nonwork-related asthma as half of these subjects were atopic. This is corroborated by the very high prevalence (54%) of a self-reported family history of atopy in the overall study population. Subjects with polysensitisation to common aeroallergens also had a six-fold higher odds ratio of presenting with AA. Among the work-related asthma phenotypes, atopy was significantly associated (OR 4.1) with probable OA but not WAA. This association between atopy and OA due to high molecular weight sensitisers, such as bakery allergens, has been well documented in the literature [27]. Polysensitised workers were also more likely to be sensitised to occupational allergens (OR 9.5) and present with OA (OR 5.5). This is consistent with the findings of studies among subjects with nonwork-related asthma in adults as well

as children, in which only a small proportion of monosensitised individuals become symptomatic when compared with the majority of symptomatic individuals that are polysensitised to common inhalant allergens [28].

In our study of bakery workers, a self-reported history of recurrent chest infections in childhood was a significant predictor (OR 5.5) of only the WAA phenotype. The association between childhood infections and asthma has been previously demonstrated by ARSHAD *et al.* [29] in their study of children of 10 yrs of age with wheeze and asthma. A more recent study among adults has also demonstrated that having frequent lower respiratory tract infections in childhood is a significant contributory factor in predicting FEV₁ decrements in adulthood [30]. Our findings therefore suggest that a history of recurrent infections in childhood could be used as an indicator to identify workers requiring more intensive surveillance, who might be at increased risk of developing WAA. The possibility of recall bias in our study cannot, however, be excluded.

Upper airway symptoms and, more specifically, work-related ocular-nasal symptoms were also significant predictors of AA and OA phenotypes in our study. Previous studies have shown that overall 11.5% of subjects with occupational rhinitis develop OA, and specifically 11.6% of those exposed to flours, grains and fodders [31]. Comorbid rhinitis or rhino-conjunctivitis has been reported in a greater proportion (45–90%) of subjects suffering from IgE-associated OA and has been attributable to various sensitisers including flour dust [27]. Interestingly, work-related ocular-nasal symptoms also appear to be an important risk factor for WAA in our study, which, as far as we can establish, has not been previously reported. The cross-sectional nature of our study does not permit conclusions about the temporal relationship of ocular-nasal symptoms and the development of asthma. Overall, however, these findings are consistent with other reported studies in the literature that indicate rhinitis to be a significant risk factor for adult-onset asthma in both work-related and nonwork-related disease outcomes, and that the appearance of ocular-nasal symptoms could be used to identify workers at greater risk of developing OA [31–33].

Self-reported work exposures, particularly episodes of high exposures, can be a useful marker in predicting recent onset adult asthma. In our study, a past history of episodes of high exposure to dusts, fumes and vapours causing asthma symptoms was a significant predictor for WAA and OA phenotypes among bakery workers. Interestingly, a stronger association was observed in workers with WAA (OR 5.8) than those with OA (OR 2.8). This finding is consistent with results from Finland in which 21% of respondents reported work-aggravated symptoms on a weekly basis in the past month in response to a number of factors including airborne dusts, gases or fumes [34]. A recently published ECRHS article also demonstrated an increased asthma risk (OR 3.3) among subjects following acute symptomatic inhalation accidents [3]. These findings suggest that high exposures to sensitisers can contribute substantially to new-onset asthma, and that workers with inhalation accidents should therefore be monitored closely over a longer period of time to identify this entity at an early stage. However, it needs to be borne in mind that

the definition used in our study, as outlined in the ECRHS protocol, has its limitations as it does not specifically differentiate between flour dust and irritants.

In our study, current job status was a significant predictor of OA in that workers with OA were more likely to be supervisors/managers (OR 4.0). Although elevated odds ratios were obtained for bakers (OR 1.6), this association was not significant. This is highly indicative of selection effects, as our pilot environmental exposure studies have shown that bakers have much higher exposures to inhalable dust than supervisors/managers. As the response rate of individual bakeries in our study was high (90–100%), it is unlikely that nonresponse bias may have affected the results. The “healthy worker effect” is a more likely explanation, in that we have noted that bakers with OA are more likely to be transferred from their high exposure jobs to less exposed jobs (supervisors/managers) rather than the least exposed jobs (counterhands). This is due to the company policy on placement of workers that ensures these bakers, often having the longest service, are retained in the bakery work environment due to their experience, which is then utilised in supervisory and managerial duties.

One of the intriguing findings of our study was the strong association (OR 6.4) between self-reported ingestion-related adverse reactions to grain products and OA phenotype, which was particularly pronounced amongst nonatopic asthmatics. The evidence for an association between wheat-related food allergy and baker's asthma is inconclusive. Some studies suggest that inhalant wheat allergy is caused by water-soluble proteins (albumins and globulins) whereas ingestion-related wheat allergy is related to nonwater-soluble, thermo-resistant gluten fractions [35]. Other studies have suggested that similar allergens are responsible for symptoms following both ingestion and inhalation of cereals [36]. MITTAG *et al.* [37] demonstrated that subjects with baker's asthma and adults with food allergy had intense IgE-reactivity to both the albumin/globulin and glutenin fraction of wheat proteins [37]. While this may explain the association in the atopic group in our study, it is possible that the stronger associations observed in the nonatopic group may be due to other factors, such as water-insoluble proteins (wheat gliadins) [38], or nonimmune reactions, such as gluten intolerance. Further studies are currently being conducted to evaluate this differential response between atopic and nonatopic asthmatics with OA and ingestion-related reactions to grain products, as this may have important implications for dietary counselling of workers with OA.

In conclusion, our study has demonstrated that OA is the most common asthma phenotype among supermarket bakery workers in this region and is an important globally evolving trend. Analysis of risk factors contributes towards differentiating between these various phenotypes. Defining various clinical phenotypes using specific clinical criteria is important for decisions regarding medical surveillance and clinical management of this high-risk group. Medical surveillance programmes in bakeries can therefore use these criteria to identify persons at risk at an early stage and intensify surveillance and other workplace interventions. Furthermore, in view of the increase in baking activities in supermarkets globally, measures to monitor and reduce exposures remain an important priority.

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STATEMENT OF INTEREST

A statement of interest for D. Heederik can be found at www.erj.ersjournals.com/misc/statements.dtl

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CHAPTER 4

**SENSITISATION TO WHEAT IS A MAJOR DETERMINANT OF
ELEVATED EXHALED NITRIC OXIDE IN BAKERS.**

University of Cape Town

CHAPTER 4

Sensitisation to wheat is a major determinant of elevated exhaled nitric oxide in bakers.

Paper overview

This paper documents the baseline fractional exhaled nitric oxide (FeNO) results in workers exposed to flour dust. Studies of the relationship between FeNO and baker's allergy and asthma are scant. This is the first detailed analysis of factors associated with changes in FeNO in bakery workers.

Contribution to the thesis and novelty

This paper addresses the second objective of this thesis. Studies of the relationship between FeNO and baker's allergy and asthma are scant. This is the first detailed analysis of factors associated with changes in FeNO in bakery workers known to be at increased risk of developing occupational allergy and asthma.

Role of the candidate

The candidate designed the study, and was responsible for data collection and data management. The candidate led the research team; designed all the questionnaires and all other data collection sheets. The candidate was involved in the data collection process, data management, quality control of the fieldwork and solely conducted all the data analysis. The candidate was responsible for drafting the manuscript and incorporating comments from collaborators, as well as final submission of the manuscript.

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Appendices related to this paper

Appendix 6: Informed consent

Appendix 7: Questionnaire

University of Cape Town

ORIGINAL ARTICLE

Sensitisation to cereal flour allergens is a major determinant of elevated exhaled nitric oxide in bakers

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ABSTRACT

Objective Various studies of the usefulness of fractional exhaled nitric oxide (FeNO) in occupational settings remain inconclusive. The objective was to investigate the determinants of increased FeNO in bakery workers.

Methods A cross-sectional study of 424 supermarket bakery workers used a questionnaire and serum specific IgE to wheat, rye and α -amylase. FeNO during the work shift were assessed using a hand-held portable sampling device (NIOX MINO).

Results The median FeNO was 15 ppb, in atopics 21 ppb and current smokers 12 ppb. Increased FeNO was strongly associated with IgE to wheat independent of smoking and atopy status. In the multivariate model, IgE to wheat, current smoking, atopy and age were significantly associated with FeNO. Stratified analysis in a subgroup of atopic non-smokers demonstrated the strongest relationship between FeNO and various clinical endpoint such as wheat (OR=9.43) or rye (OR=11.76) sensitisation, work-related allergic rhinitis (OR=8.13) or asthma (OR=5.44), and probable baker's asthma (OR=6.72).

Conclusions Sensitisation to cereal flour allergens rather than asthma symptoms is a major determinant of elevated FeNO among bakers. This relationship is modified by atopy and current smoking status.

BACKGROUND

Various studies have demonstrated that the measurement of fractional exhaled nitric oxide (FeNO) is a useful non-invasive method for assessing eosinophilic inflammatory airway disease.¹ It is widely accepted that airway inflammation is associated with occupational asthma and rhinitis; however, the sensitivity and specificity of FeNO have not been sufficiently assessed in occupational settings.² While the predictive value of FeNO has been shown to be higher than spirometry or peak expiratory flow,³ more studies are required to examine the effectiveness of FeNO in the early detection of respiratory disease due to workplace exposures.⁴

There is currently conflicting evidence in the literature concerning the role of FeNO in occupational asthma, and hence the need to clarify the interpretation of changes in FeNO following exposure to occupational agents.⁴ FeNO has been demonstrated as a useful marker of exposure to gases and dusts in construction workers,⁵ organic solvents in leather workers⁶ and among aluminium potroom workers.⁷ Exhaled nitric oxide is also reported to be elevated

What this paper adds

- ▶ Studies of the relationship between FeNO and baker's allergy and asthma are scant.
- ▶ This is the first detailed analysis of factors associated with changes in FeNO in supermarket bakery workers known to be at an increased risk of developing occupational allergy and asthma.
- ▶ This study demonstrated that sensitisation to cereal flour allergens, rather than asthma symptoms, is a major determinant of elevated FeNO among bakers.
- ▶ The strong relationship between FeNO and sensitisation to cereal flour allergens is modified by atopy and current smoking status.

in workers exposed to organic dusts,⁸ laboratory animal workers⁹ and workers in swine confinement buildings.¹⁰ The FeNO increase in the latter group was demonstrated 5 h after exposure. In another study, Baur and Barbinova¹¹ demonstrated a greater than 50% increase in asthmatic healthcare workers 22 h after specific inhalation challenge to latex. However, other studies on the impact of swine dust exposure showed no apparent effect on FeNO¹² while other studies showed no clear relationship between FeNO in subjects exposed to latex or isocyanates.¹³ Recently, a strong association was reported in a subgroup of non-smoking, non-atopic farmers and agricultural processing workers exposed to endotoxin.¹⁴ Studies have also demonstrated an increase in FeNO in relation to immunoglobulin (Ig)E sensitisation¹⁵ and allergen exposure,¹⁷ and a decrease in FeNO with allergen avoidance.¹⁸ A recent review concluded that FeNO is a signal of allergen-triggered Th2-driven inflammatory mechanisms within the bronchial mucosa and can be considered as a marker of allergen exposure in sensitised subjects.¹⁹

Studies on the relationship between FeNO and asthma outcomes in bakers are scant. A study among bakers, farmers and healthcare workers showed a significant increase in FeNO only 24 h after a specific inhalation test²⁰ while a 15-month follow-up study among apprentice bakers demonstrated that an increase in FeNO correlated with the occurrence of bronchial hyperresponsiveness.²¹ Recently, a study by Pedrosa *et al*²² demonstrated an increase in

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FeNO levels 24 h after allergen exposure in subjects with a positive bronchial allergen challenge with high-molecular weight agents, including cereal flour.

The aim of this study was to evaluate the determinants of FeNO for various clinically relevant endpoints in baker's allergy and asthma.

METHODS

Study design, population and sampling

A cross-sectional study was conducted on 424 workers in 31 supermarket bakeries of a supermarket chain store in the Western Cape province of South Africa. This is a follow-up investigation of a previous study of 517 workers originally assessed as part of a medical surveillance programme for baker's allergy and asthma. At follow-up 3 years later, 93 workers from the original cohort were no longer working in the bakery and were not traceable for further evaluation. Ethical clearance of the protocol was obtained from the University of Cape Town prior to the study being conducted.

Questionnaire

Each worker answered a questionnaire which included a history of recent chest infections, asthma symptoms, rhinitis and work-related respiratory symptoms. Information was also obtained on alcohol use, medication use, exercise and dietary history (nitrate rich foods). Smoking status was classified into two categories, that is, non-smoker as lifelong abstinence from smoking and current smoker (currently smoking for as long as a year). Symptoms were considered to be work-related if they were reported to have worsened during the work shift as reported previously.²³

Immunological tests

Quantification of serum specific IgE antibodies CAP-FEIA (fluorescence enzyme immuno assay) was performed using the ImmunoCAP 100 System (Phadia, Uppsala, Sweden) using wheat flour (f4), rye flour (f5) and fungal α -amylase (k87) according to the manufacturer's instructions. The presence of atopy in workers who did not undergo skin prick tests (SPTs) was defined by a positive Phadiatop test (ImmunoCAP 100 System; Phadia). An ImmunoCAP result of ≥ 0.35 kU_A/l was regarded as positive.²³

SPTs were performed using the following standard common local aeroallergens (ALK-Abello' A/S, Horsholm, Denmark): house dust mite (*Dermatophagoides pteronyssinus*), bermuda grass (*Cynodon dactylon*), rye grass (*Lolium perenne*), grass mix (Pollen III: Avena, Hordeum, Triticum, Secale), cockroach (*Blattella germanica*), cat (*Felis domesticus*), dog (*Canis familiaris*), mould mix (*Cladosporium herbarum*, *Alternaria alternata*, *Fusarium*) and *Aspergillus* (*Aspergillus fumigatus*) as previously reported.²³ For the purposes of this study, atopy was considered to be present if the SPT to one or more common aeroallergens was positive.

Exhaled FeNO tests

A hand-held portable sampling device (NIOX MINO) was used to determine FeNO during the work shift according to American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations.^{24 25} The tests were conducted during the work shift at the various supermarket bakery stores in a distant room removed from the bakery area. Testing of workers occurred throughout the working week and work shift, with no particular variation with regard to time of testing for the different jobs. Three technically adequate FeNO were measured and

an average determined. Special instructions were given to workers to refrain from smoking, eating or drinking (at least 1 h) before the test. This was confirmed prior to testing, and those who did not follow the instructions were tested at a later stage after establishing their full compliance with these instructions.

Statistical analysis

Statistical analysis was performed using STATA V8.²⁶ Linear regression models were developed to describe the determinants of variability in FeNO. The natural logarithm (ln) of the measured FeNO average was used as the dependent variable since the data followed a log-normal distribution. Multiple linear regression was performed with variables that had an r^2 value of 0.01 or greater and a p value of 0.1 or less in the univariate analyses. Simultaneous quantile regression was also performed to determine the effect of the predictor variables for different levels (centiles) of FeNO. A p value of 0.10 was used as criterion to determine the best predictive model for FeNO, using stepwise forward and backward model selection procedure. This analysis included all predictor variables for FeNO that were significant in the univariate regression analysis, which resulted in some variables not remaining in the final model. The strength of the associations were summarised using multiple logistic regression stratified by atopy and smoking, with a cut-off of >25 ppb defined as abnormal.²⁵

RESULTS

Characteristics of subjects

A total of 424 currently employed workers participated in the study. The population comprised bakers (40%), counterhands (26%), confectioners (7%), supervisors/managers (14%) and ex-bakers (13%) who were removed from the bakery and transferred to other departments. Other characteristics of the study population are outlined in table 1. Work-related (WRS) ocular-nasal symptoms (44%) were more prevalent than chest symptoms (26%). A higher proportion of workers were sensitised to wheat (31%) or rye (28%) than to fungal α -amylase (2%). Sensitisation to wheat and rye were highly correlated ($r=0.83$, $p<0.001$). There were 6% of workers with probable baker's asthma (WRS, specific allergic sensitisation and previous history of a positive methacholine challenge test), based on the findings of our initial survey.²³ Stratified analysis across job categories revealed a higher prevalence of work-related chest symptoms among counterhands in comparison with bakers (table 2). However, the prevalence of sensitisation to occupational allergens was higher for bakers than for counterhands. No significant differences were observed for FeNO levels across job categories.

In a subgroup analysis of SPT data the prevalence of sensitisation was the highest to storage mite (19%), followed by rye grass (18%), grassmix (17%) and bermuda grass (11%). The overall prevalence of sensitisation to any grass pollen (rye grass, bermuda grass and grass mix) was 25%. Among those sensitised to wheat and/or rye, only 48% were also cosensitised to grass pollen.

Among subjects with cereal flour sensitisation based on allergen specific IgE ($n=138$), there were 31 (22%) and 79 (57%) subjects respectively who reported allergic asthma and rhinitis, while a greater proportion, 57 (41%) and 87 (63%), of subjects reported work-related allergic asthma and rhinitis.

The median FeNO was 15 ppb (range: 4–251); 74% had low FeNO (<25 ppb) levels, 15% intermediate (25–50 ppb) levels and 11% high (>50 ppb) levels.²⁵ Atopics had significantly

Workplace

Table 1 Univariate analysis of factors associated with fractional exhaled nitric oxide (FeNO) (ln) levels among bakery workers

Factor	N=424	β	r^2	p Value
Demographic and personal factors				
Age (years)	32 (27–40)	−0.0132	0.0198	0.004
Gender (M:F)	43:57	0.2134	0.0170	0.007
Height (m)	1.65 (1.59–1.72)	0.7438	0.0064	0.186
Weight (kg)	74 (61–90)	−0.0039	0.0087	0.056
BMI (kg/m ²)	28 (23–33)	−0.0080	0.0051	0.237
Atopy	109 (39%)	0.5572	0.1088	<0.001
Blood pressure				
Systolic (mm Hg)	120 (110–127)	0.0022	0.0017	0.396
Diastolic (mm Hg)	76 (67–85)	0.0006	0.0001	0.823
Hypertension*	84 (20%)	−0.0234	0.0001	0.813
Smoking†	183 (43%)	−0.4496	0.0754	<0.001
Number of cigarettes smoked per day	6 (4–10)	−0.0237	0.0191	0.061
Cigarettes/day <5	53 (13%)	0		
Cigarettes/day 5–9	71 (17%)	−0.3261	0.0408	0.020
Cigarettes/day ≥10	59 (14%)	−0.3657	0.0408	0.012
Recent alcohol intake‡	27 (6%)	−0.1596	0.0023	0.324
Recent vegetable intake‡	89 (21%)	0.0096	0.0000	0.921
Recent exercise‡	29 (7%)	0.3203	0.0099	0.040
Steroid use	16 (4%)	0.2722	0.0041	0.189
Recent lung function test‡	3 (1%)	−0.3600	0.0014	0.445
Recent chest infection§	177 (42%)	0.1592	0.0094	0.046
Occupational history				
Counterhands	148 (31%)	0		
Confectioners	34 (7%)	−0.2641	0.0144	0.123
Supervisor/managers	68 (14%)	0.1257	0.0144	0.338
Bakers	234 (48%)	−0.0793	0.0144	0.422
High dust exposure job¶	310 (74%)	−0.0228	0.0002	0.801
Employment duration on bakery	7±5	−0.0132	0.0063	0.187
Employment duration in current job	4±4	−0.0116	0.0030	0.368
Symptom history in past 12 months				
Hayfever	153 (36%)	0.2477	0.0215	0.002
Dry cough	129 (30%)	−0.0319	0.0003	0.711
Shortness of breath	118 (28%)	−0.1776	0.0096	0.043
Chest tightness	110 (26%)	−0.0691	0.0014	0.443
Wheezing	87 (21%)	−0.1037	0.0027	0.289
Doctor diagnosed asthma	40 (9%)	0.1943	0.0049	0.150
Work-related symptoms				
Chest	111 (26%)	0.0716	0.0015	0.426
Ocular–nasal	187 (44%)	0.0946	0.0033	0.235
Serum specific IgE				
Wheat IgE (kU/l)	0.07 (0.04–0.70)	0.0196	0.0999	<0.001
Rye IgE (kU/l)	0.06 (0.03–0.65)	0.0142	0.1201	<0.001
Fungal α -amylase	0.001 (0.00–0.10)	0.0878	0.0104	0.036
Serum specific IgE				
Wheat IgE (>0.35 kU/l)	131 (31%)	0.5849	0.1110	<0.001
Class I: >0.35–<0.7	25 (6%)	0.2806	0.1546**	0.074
Class II: 0.7–<3.5	43 (10%)	0.4786	0.1546**	<0.001
Class III: 3.5–<17.5	40 (9%)	0.6272	0.1546**	<0.001
Class IV: 17.5–<50	14 (3%)	0.8988	0.1546**	<0.001
Class V: 50–<100	5 (1%)	1.0181	0.1546**	0.003
Class VI: ≥100	3 (1%)	2.0737	0.1546**	<0.001

Continued

Table 1 Continued

Factor	N=424	β	r^2	p Value
Rye IgE (>0.35 kU/l)	119 (28%)	0.5742	0.1012	<0.001
Class I: >0.35–<0.7	16 (4%)	0.4852	0.1533**	0.012
Class II: 0.7–<3.5	38 (9%)	0.3041	0.1533**	0.019
Class III: 3.5–<17.5	30 (7%)	0.3742	0.1533**	0.010
Class IV: 17.5–<50	16 (4%)	0.8567	0.1533**	<0.001
Class V: 50–<100	9 (2%)	1.2320	0.1533**	<0.001
Class VI: ≥100	10 (2%)	1.2992	0.1533**	<0.001
Fungal α -amylase IgE (>0.35 kU/l)	7 (2%)	0.6033	0.0090	0.051
Class I: >0.35–<0.7	2 (0.5%)	0.6912	0.0145	0.229
Class II: 0.7–<3.5	2 (0.5%)	−0.1044	0.0145	0.856
Class III: 3.5–<17.5	3 (0.5%)	1.0165	0.0145	0.031
Cereal flour sensitisation††	138 (33%)	0.5521	0.1017	<0.001
Allergic symptoms‡‡				
Work-related allergic rhinitis	87 (21%)	0.4727	0.0554	<0.001
Work-related allergic asthma	57 (13%)	0.3938	0.0274	0.001
Probable baker's asthma	27 (6%)	0.1790	0.0029	0.268

Median and inter-quartile range presented for continuous variables since data skewed.

*Systolic ≥140 and/or diastolic ≥90.

†Currently smoking for as long as a year.

‡Recent=1 day ago.

§Self-reported flu or sinusitis in the past 3 weeks.

¶High dust exposure jobs=bakers, confectioners, managers and supervisors versus low dust exposed job category of counterhands.

** r^2 represents one model.††Cereal flour sensitisation=sensitised to wheat, rye or α amylase on IgE (>0.35 kU/l).

‡‡Allergic symptoms=self-reported work-related symptoms in the presence of cereal flour sensitisation.

BMI, body mass index.

higher FeNO than non-atopics (median 21 vs 13 ppb; $p<0.001$), while current smokers had significantly lower FeNO (median 12 vs 19 ppb; $p<0.001$).

Correlation between FeNO and IgE

A modest positive correlation was observed between FeNO and log(n) wheat IgE ($r=0.36$; $p<0.001$). Stratification by atopic status revealed similar correlations for atopics ($r=0.30$; $p=0.001$) and non-atopics ($r=0.31$; $p<0.001$). Similar significant correlations were demonstrated between FeNO and rye specific IgE, while the relationship for fungal α amylase was weaker overall ($r=0.19$; $p=0.004$), and not significant when stratified by atopic status.

Factors associated with variability in FeNO

Host factors such as current smoking ($\beta:-0.4496$) and age ($\beta:-0.0132$) were associated with lower FeNO, while atopy ($\beta:0.5489$), recent exercise ($\beta:0.3203$), male gender ($\beta:0.2134$) and recent chest infections ($\beta:0.1592$) were associated with increased FeNO (table 1). A self-reported history of hayfever ($\beta:0.2477$, $p=0.002$), but not work-related upper ($\beta:0.0716$; $p=0.235$) or lower respiratory symptoms ($\beta:0.0946$; $p=0.426$) were associated with higher FeNO. However, allergic work-related upper ($\beta:0.4727$, $p\leq0.001$) as well as lower respiratory symptoms ($\beta:0.3938$, $p=0.001$) were significantly associated

Table 2 Prevalence of sensitisation, work-related symptoms and fractional exhaled nitric oxide (FeNO) levels by job category among bakery workers

Outcome	Job category			
	Counterhand (n=109)	Supervisor/managers (n=58)	Confectioners (n=28)	Bakers (n=172)
Work-related symptoms				
Chest	27 (25%)	15 (26%)	4 (14%)	32 (18%)
Ocular–nasal	42 (39%)	22 (38%)	6 (21%)	72 (42%)
FeNO				
Low <25 ppb	79 (72%)	38 (65%)	24 (86%)	135 (78%)
Medium 25–50 ppb	20 (18%)	8 (14%)	3 (11%)	20 (12%)
High >50 ppb	10 (10%)	12 (21%)	1 (3%)	17 (10%)
Serum specific IgE				
Wheat (>0.35 kU/l)	20 (18%)	17 (29%)	9 (32%)	53 (31%)
Rye (>0.35 kU/l)	21 (19%)	16 (28%)	6 (21%)	45 (26%)
Fungal α -amylase (>0.35 kU/l)	0 (0%)	2 (3%)	0 (0%)	3 (2%)
Allergic respiratory symptoms				
Work-related allergic rhinitis	14 (13%)	11 (19%)	2 (7%)	29 (17%)
Work-related allergic asthma	7 (6%)	8 (14%)	3 (11%)	12 (7%)

with elevated FeNO. A greater increase in the β estimate was demonstrated for IgE to fungal α -amylase (β :0.0878) than to wheat (β :0.0196), or rye (β :0.0142).

A subgroup analysis of the relationship between sensitisation to common aeroallergens and FeNO demonstrated strong positive associations for rye grass (β :0.3672), grass mix (β :0.3915), storage mite (β :0.3354) and grass pollen (β :0.3551, $p=0.002$).

After adjusting to control for sensitisation to mites and grass pollen (ryegrass, grassmix, bermuda grass), there was an even stronger association between FeNO and sensitisation and to wheat (adjusted β :0.6897, $p<0.001$; unadjusted β :0.5849, $p<0.001$) and rye (adjusted β :0.6993, $p<0.001$; unadjusted β :0.5742, $p<0.001$).

There was no association demonstrated between FeNO and either occupational category or employment duration.

In the simultaneous quantile regression analysis atopy, smoking, recent chest infections, a history of hayfever and serum specific IgE to flour allergens (wheat, rye) were consistently associated with FeNO at each quantile (0.25, 0.50, 0.75) (data not shown). Although no association was demonstrated in the overall simple linear regression model at the upper quantile (0.75), a strong positive relationship was found for both doctor diagnosed asthma (β :0.6074; $p=0.004$) and probable baker's asthma (β :0.6329; $p=0.001$) with FeNO.

In the final multiple linear regression model including all variables significantly associated with FeNO in the univariate analysis, only IgE to wheat, current smoking, atopy and age remained significantly associated with FeNO (table 3) using a

stepwise model building approach. Due to the high correlation between sensitisation to wheat and rye ($r=0.83$), sensitisation to the latter allergen did also not appear in the final model. In this final model, IgE to wheat accounted for most of the variability in FeNO (15%) followed by smoking (6%) and atopy (5%). The β estimate increased by 0.2 with each class increase in wheat IgE level up to class 5 and was even more pronounced for class 6.

Predictors of elevated FeNO in logistic regression models

In the stratified logistic models, for atopy and smoking, a strong relationship was found for workers with elevated FeNO (>25 ppb) and sensitisation to wheat or rye, but not with fungal α -amylase, due to lack of power (table 4). A strong association was observed between FeNO and work-related allergic rhinitis irrespective of smoking and atopic status. However, the association with probable baker's asthma was only evident in non-atopics. Although the relationship between elevated FeNO and sensitisation to wheat was similar in both atopics and non-atopics, a stronger association was observed for non-atopics (OR=6.4) than atopics (OR=3.3) sensitised to rye.

Analysis for a possible interaction between atopy and smoking demonstrated strong positive associations with FeNO among atopic non-smokers for various clinical endpoints such as wheat (OR=9.43) or rye (OR=11.76) sensitisation, work-related allergic rhinitis (OR=8.1) or asthma (OR=5.4) and probable baker's asthma (OR=6.7) (table 5). The analysis further showed that the effect of smoking on FeNO appears to override atopy, demonstrating a clear dose-dependent effect with increasing number of cigarettes smoked per day.

DISCUSSION

This study, to our knowledge, represents the first detailed analysis of factors associated with FeNO among workers exposed to flour dust in supermarket bakeries, and one of few reported for bakery workers overall.^{20 21}

Normative values for FeNO have been reported in a number of different populations ranging between 27 and 57 ppb for non-asthmatics.²⁵ In comparison with these studies, FeNO in our study (90% upper limit: 57 ppb) was much higher than the levels reported by Travers *et al*¹⁵ in a random community survey (90% upper limit: 41 ppb) but similar to levels reported by

Table 3 Multiple linear regression model of fractional exhaled nitric oxide (ln) predictors among bakery workers

Factor	Estimate (β)	95% CI	p Value
Wheat	0.4746	0.28 to 0.67	<0.001
Current smoker	-0.4550	-0.63 to -0.28	<0.001
Atopy	0.3442	0.16 to 0.53	<0.001
Age	-0.0121	-0.02 to -0.01	0.023

Overall multiple regression model, $\beta_0=3.2$, $p<0.001$, cumulative $r^2=0.2573$.

Table 4 Predictors of elevated fractional exhaled nitric oxide (FeNO) (>25 ppb) stratified by atopy and smoking among bakery workers in separate multiple logistic regression models

Predictor	Smoking (OR, CI)*		Atopy (OR, CI)*	
	Smoker	Non-smoker	Atopic	Non-Atopic
General symptoms				
Wheeze	1.5 (0.6 to 3.5)	1.5 (0.7 to 3.1)	1.4 (0.6 to 3.5)	1.2 (0.5 to 3.3)
Hayfever	2.6 (1.1 to 6.3)	1.9 (1.1 to 3.5)	1.9 (0.8 to 4.9)	1.8 (0.7 to 4.4)
Doctor diagnosed asthma	2.1 (0.7 to 6.9)	3.2 (1.2 to 8.4)	2.4 (0.8 to 6.8)	3.1 (0.9 to 9.6)
Work-related symptoms				
Chest	1.0 (0.4 to 2.5)	1.5 (0.8 to 2.9)	0.8 (0.4 to 1.8)	1.7 (0.7 to 4.4)
Ocular–nasal	1.2 (0.5 to 2.7)	1.0 (0.6 to 1.8)	1.3 (0.6 to 2.9)	1.0 (0.4 to 2.4)
Allergic symptoms				
Work-related allergic rhinitis	3.2 (1.4 to 7.7)	2.9 (1.5 to 5.6)	2.8 (1.2 to 6.6)	4.1 (1.5 to 11.4)
Work-related allergic asthma	2.5 (0.9 to 6.9)	2.3 (1.1 to 5.0)	1.8 (0.7 to 4.4)	2.4 (0.7 to 8.0)
Serum specific IgE				
Wheat (>0.35 kU/l)	3.5 (1.5 to 7.9)	3.8 (2.1 to 6.9)	3.9 (1.7 to 9.5)	4.1 (1.6 to 10.3)
Rye (>0.35 kU/l)	3.7 (1.6 to 8.7)	4.4 (2.4 to 7.9)	3.2 (1.4 to 7.3)	6.5 (2.5 to 16.4)
Fungal α amylase (>0.35 kU/l)	2.6 (0.2 to 35.7)	†	2.9 (0.4 to 19.4)	†
Cereal flour sensitisation	3.1 (1.4 to 7.1)	4.0 (2.3 to 7.2)	3.8 (1.6 to 9.2)	5.0 (2.0 to 12.5)
Probable baker's asthma	1.5 (0.4 to 6.2)	2.4 (0.8 to 7.1)	0.8 (0.3 to 2.5)	4.3 (1.1 to 16.3)

*Adjusted for age and recent chest infection.

†Undefined since none of the subjects had elevated FeNO (>25 ppb).

Olin *et al.*¹⁶ With particular reference to studies in occupational populations, the median and/or mean FeNO in the current study of bakery workers were also higher than levels reported in other studies of workers exposed to endotoxins,¹⁴ organic dust,¹⁰ laboratory animals⁹ and latex,¹¹ irrespective of smoking and atopic status. This could be attributed to differences in timing of measurements, exposure duration of subjects, and inclusion and exclusion criteria based on symptom history use in different studies, unlike the current study that included all workers.

In this study, the major determinants for FeNO aside from serum specific IgE to wheat or rye were gender, age, smoking, atopy, recent chest infections, hayfever and allergic upper and lower respiratory symptoms. The higher FeNO in male subjects is consistent with several studies reporting similar findings.^{15–25} The association between FeNO levels and height as with other variables has been inconsistent in studies such as Sandrini *et al.*²⁷ FeNO also correlates strongly with atopy as had been observed in large cohort studies^{15–28} while higher FeNO has been observed in asymptomatic subjects with atopy, other studies only demonstrating this association in subjects with asthma or rhinitis.²⁹ In the current study, no significant association was observed between elevated FeNO (>25 ppb) and hayfever or asthma irrespective of atopic status, although in the unadjusted models hayfever, but not asthma, showed a positive relationship. However, in the current study, work-related allergic rhinitis was consistently positively associated with an elevated FeNO in the unadjusted models irrespective of atopic status. The findings are consistent with the study of Travers *et al.*¹⁵ in which allergic rhinitis was associated with higher FeNO.

While age appears to be an important determinant in children, there is less agreement in studies among adults. The finding of the current study, among a relatively young adult workforce, showing an inverse relationship with FeNO is at variance with other studies showing a positive association between age and FeNO. The possibility of selection bias cannot be excluded due to the cross-sectional nature of the study. Olin

*et al.*¹⁶ found an independent positive relationship with age, with the oldest group (>64 years) having 40% higher FeNO compared with the youngest group, while Franklin *et al.*³⁰ also found that FeNO increased with age. However, a study from Hong Kong found no correlation ($r=0.12$; $p=0.17$) between age and FeNO.³¹

The current study showed a significant decrease in FeNO among smokers even after adjusting for other potential confounders. It is well described that smoking leads to a decrease in FeNO³² and that smoking cessation may result in an increase in FeNO.³³ In multivariate linear models, the overall estimate of FeNO corresponding to smoking varied between $\beta=-0.7$ and $\beta=-0.8$ for smokers compared with non-smokers.^{15–16} However, smoking effect was not as strong in our study ($\beta=-0.45$). Furthermore, a strong association between elevated FeNO and doctor-diagnosed asthma was only observed among non-smokers as reported previously,¹⁶ despite asthmatic smokers having a higher FeNO compared with asthmatic non-smokers in this and other studies.³⁴

In the current study, no significant association was demonstrated between occupation and FeNO. This lack of association with occupation (high dust exposure jobs vs low dust exposure) could be explained by the possible delayed reaction of increase in FeNO following allergen exposure relating to timing of measurements. In this current study, due to logistical considerations only one cross-sectional measurement was done, although two consecutive measurements would have been more appropriate to determine an increase in FeNO following allergen exposure. This increase in FeNO has been documented by Pedrosa *et al.*²² 24 h after allergen exposure and Swierczyńska-machura *et al.*²⁰ after specific inhalation challenge. Another possible explanation for this finding could be possible exposure misclassification since job titles, instead of actual environmental measurements, were used as a proxy for exposure in this study. Although individuals had different job titles, the open plan design of the bakery resulted in possible increased exposures in individuals not directly involved in the baking process. Future studies should

Table 5 Predictors of elevated fractional exhaled nitric oxide (>25 ppb) among bakery workers in multiple logistic regression models exploring interaction between smoking and atopy

Predictor	Atopic Smoker (OR, CI)*	Atopic Non-smoker (OR, CI)*	Non-atopic Smoker (OR, CI)*	Non-atopic Non-smoker (OR, CI)*
Work-related chest symptoms	1.55 (0.62 to 3.86)	4.26 (2.03 to 8.93)	0.39 (0.17 to 0.92)	1.08 (0.59 to 1.99)
Cigarettes/day <5	1.42 (0.33 to 6.14)	†	0.49 (0.14 to 1.76)	†
Cigarettes/day 5–9	0.82 (0.13 to 5.15)	†	0.28 (0.05 to 1.62)	†
Cigarettes/day ≥10	0.47 (0.05 to 4.84)	†	0.16 (0.12 to 1.61)	†
Work-related ocular–nasal symptoms	1.47 (0.58 to 3.72)	4.04 (1.94 to 8.40)	0.37 (0.16 to 0.86)	1.01 (0.57 to 1.81)
Cigarettes/day <5	3.29 (0.72 to 15.11)	†	1.13 (0.35 to 3.66)	†
Cigarettes/day 5–9	1.92 (0.31 to 11.82)	†	0.66 (0.14 to 3.19)	†
Cigarettes/day ≥10	1.12 (0.12 to 10.60)	†	0.38 (0.05 to 3.10)	†
Wheat (>0.35 kU/l)	3.66 (1.41 to 9.48)	9.43 (4.44 to 20.04)	1.62 (0.66 to 3.95)	4.16 (2.19 to 7.92)
Cigarettes/day <5	4.74 (1.13 to 19.87)	†	2.45 (0.69 to 8.78)	†
Cigarettes/day 5–9	2.50 (0.41 to 15.26)	†	1.29 (0.23 to 7.28)	†
Cigarettes/day ≥10	1.32 (0.13 to 13.54)	†	0.68 (0.07 to 6.79)	†
Rye (>0.35 kU/l)	4.19 (1.59 to 11.07)	11.76 (5.26 to 26.27)	1.60 (0.68 to 3.78)	4.50 (2.40 to 8.43)
Cigarettes/day <5	4.96 (1.14 to 21.23)	†	2.06 (0.61 to 6.96)	†
Cigarettes/day 5–9	2.52 (0.41 to 15.57)	†	1.05 (0.20 to 5.61)	†
Cigarettes/day ≥10	1.29 (0.13 to 13.14)	†	0.53 (0.06 to 5.08)	†
Cereal flour sensitisation	3.89 (1.49 to 10.17)	10.33 (4.78 to 22.35)	1.68 (0.69 to 4.08)	4.46 (2.35 to 8.48)
Cigarettes/day <5	4.36 (1.01 to 18.82)	†	2.06 (0.56 to 7.55)	†
Cigarettes/day 5–9	2.41 (0.38 to 15.33)	†	1.14 (0.19 to 6.68)	†
Cigarettes/day ≥10	1.33 (0.12 to 14.56)	†	0.63 (0.06 to 6.54)	†
Work-related allergic rhinitis	3.11 (1.17 to 8.28)	8.13 (3.72 to 17.76)	1.13 (0.46 to 2.79)	2.97 (1.53 to 5.70)
Cigarettes/day <5	5.87 (1.11 to 30.99)	†	2.23 (0.54 to 9.20)	†
Cigarettes/day 5–9	3.48 (0.44 to 27.41)	†	1.33 (0.20 to 8.98)	†
Cigarettes/day ≥10	2.07 (0.16 to 27.35)	†	0.79 (0.07 to 9.57)	†
Work-related allergic asthma	2.01 (0.74 to 5.44)	5.44 (2.36 to 12.54)	0.61 (0.24 to 1.55)	1.65 (0.80 to 3.41)
Cigarettes/day <5	1.88 (0.37 to 9.55)	†	0.63 (0.14 to 2.78)	†
Cigarettes/day 5–9	0.97 (0.13 to 7.32)	†	0.33 (0.05 to 2.32)	†
Cigarettes/day ≥10	0.50 (0.04 to 6.34)	†	0.17 (0.01 to 2.12)	†
Probable baker's asthma	2.54 (0.85 to 7.64)	6.72 (2.50 to 18.06)	0.67 (0.24 to 1.87)	1.78 (0.75 to 4.23)
Cigarettes/day <5	1.55 (0.30 to 8.17)	†	0.61 (0.12 to 2.99)	†
Cigarettes/day 5–9	1.00 (0.15 to 6.87)	†	0.39 (0.06 to 2.61)	†
Cigarettes/day ≥10	0.65 (0.06 to 5.56)	†	0.25 (0.03 to 2.55)	†

*Adjusted for age and recent chest infection.

†Analysis only applicable for current smokers.

rather assign exposure categories based on personal exposure measurements to better evaluate the relationship between occupational exposure (job title) and FeNO. There is also the added possibility that movement of workers within the bakery from high to lower exposed jobs, due to symptoms, may have further contributed to this misclassification.

The final multivariate model explained just over a quarter ($r^2=26$) of the total variability in FeNO, suggesting that other unknown factors may contribute substantially to the variability in FeNO. Levesque *et al*³⁵ also reported an overall variability of 26% that was slightly higher than Travers *et al* (22%).¹⁵ The latter study, however, did not account for serum specific IgE in their model. It has therefore been suggested that the variation in FeNO may be caused by a complex interaction of genetic, biologic and environmental factors, not all of which are easily measurable.³⁵

Among those factors, serum specific IgE to wheat or rye was the strongest determinant of the variability in FeNO (15%) in this study. Furthermore, we found slightly higher correlations for specific IgE to wheat or rye and FeNO ($r=0.36$) in comparison with other studies that used total serum IgE ($r=0.11$), which is not as specific.¹⁵ This association has been ascribed to

asthma being predominantly an IgE-mediated allergic airways disease. However, the association appears quite modest suggesting that the association between atopy and FeNO may be due to shared genetic determinants.³⁶

Several studies indicate that smoking and atopy are major determinants of FeNO. However, few studies have investigated the effect of a possible interaction between smoking and atopy on FeNO. In a study of farmers and agricultural processing workers, Smit *et al* found a strong association between increasing endotoxin exposure and FeNO only in non-smoking, non-atopic workers.¹⁴ However, although our study also demonstrated strong associations among non-smoking, non-atopic workers, a stronger association was observed between sensitisation to wheat or rye and elevated FeNO (FeNO>25 ppb) in atopic non-smokers. Furthermore, a strong association was also observed between elevated FeNO and cereal flour-related allergic symptoms as well as probable baker's asthma in atopic non-smoking workers. It can be concluded from this study that the overall effect of smoking ($\beta=-0.4550$) on FeNO overrides atopy ($\beta=0.3442$) in a dose-dependent relationship when these characteristics coexist in bakery workers sensitised to flour allergens.

In conclusion, the present study demonstrated that sensitisation to wheat or rye, but not symptoms, is a major determinant of FeNO among bakery workers. Furthermore, a strong association was observed between FeNO and allergic upper and lower respiratory disease associated with sensitisation to cereal flour allergens. The usefulness of FeNO is increasingly being acknowledged in occupational settings when compared with sputum eosinophil count for identifying workers with asthma, as it is well tolerated, less time consuming, inexpensive, and could be performed in various workplace settings using hand-held portable sampling devices. It may therefore provide a valid alternative to sputum eosinophil counts to evaluate bronchial inflammation when sputum collection is unavailable, unfeasible or unsuccessful. However, further studies are needed to assess the usefulness of FeNO to address various diagnostic challenges in occupational contexts. These include their use in medical surveillance programmes for the early detection of work-related allergic respiratory disease as has been reported in isolated studies evaluating the effectiveness of control measures³⁷ or before and after a specific bronchial challenge when evaluating difficult cases of occupational asthma.³⁸

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Contributors MFJ was responsible for the design study and over-seeing the analysis and write up. RB was responsible for over-seeing fieldwork, data analysis and write up.

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Sensitisation to cereal flour allergens is a major determinant of elevated exhaled nitric oxide in bakers

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CHAPTER 5

EXPOSURE TO FLOUR DUST IN SOUTH AFRICAN SUPERMARKET BAKERIES: MODELING OF BASELINE MEASUREMENTS OF AN INTERVENTION STUDY.

University of Cape Town

CHAPTER 5

Exposure to flour dust in South African supermarket bakeries: Modeling of baseline measurements of an intervention study.

Paper overview

Exposure to flour dust has been reported as an important risk factor for allergic respiratory disease among bakery workers. This article presents the results of the detailed baseline exposure assessment study. It presented the distributional characteristics of inhalable flour dust, wheat, rye and fungal α -amylase allergen exposures. The variability and the sources of variation for all three measures of exposure are discussed in order to identify high risk jobs and work processes that could be prioritised for intervention.

Contribution to the thesis and novelty

This paper addresses the third objective of the thesis. Aside from the detailed exposure metrics for various allergens in supermarket bakeries an inventory of control measures currently used in these bakeries is also presented. This baseline characterisation of exposure established the basis for the intervention strategy. The results also enabled the development of predictive exposure models so as to generate exposure predictions assigned to individuals in the detailed study of exposure-response relationships.

Role of the candidate

The candidate designed the study, and was solely responsible for data collection and data management. The candidate played a key role in conducting the advanced data analysis and interpretation, supported by Dr Tim Meijster. The candidate was responsible for drafting the

manuscript and incorporating comments from collaborators, as well as final submission of the manuscript.

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Appendices related to this paper

Appendix 8: Environmental data collection sheet

University of Cape Town

Exposure to Flour Dust in South African Supermarket Bakeries: Modeling of Baseline Measurements of an Intervention Study

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Introduction: Exposure to flour dust has been reported as an important risk factor for allergic respiratory disease among bakery workers. A high prevalence of allergic sensitization and asthma was recently reported in South African supermarket bakeries. The aim of this study was to conduct a detailed exposure assessment of these bakeries so as to provide the baseline for a broader intervention study.

Methods: A total of 211 full-shift personal samples were collected on randomly selected individuals within five different job categories in 18 bakeries. The samples were analyzed for particulate mass and specific flour dust allergens (wheat, rye, and fungal alpha-amylase). Exposure models were developed using job, bakery size, tasks, and specific ingredients used. Bakery and worker were regarded as random effect components.

Results: Bread bakers had the highest average (geometric mean) exposures (1.33 mg m^{-3} flour dust particulate, $13.66 \text{ } \mu\text{g m}^{-3}$ wheat allergens, and $5.14 \text{ } \mu\text{g m}^{-3}$ rye allergens). For alpha-amylase allergens, most samples were below the limit of detection for several occupational titles. In the mixed effect models, the significant predictors of elevated exposure to inhalable dust particulate as well as wheat and rye allergen concentrations were large bakery size, bread baking, and use of cereal flours, while tasks such as confectionery work were negatively correlated with these exposure metrics. Weighing tasks and use of premix products were associated with increased exposure to fungal alpha-amylase. A high correlation between particulate dust and wheat ($r = 0.84$) as well as rye ($r = 0.86$) was observed, with a much lower correlation between particulate dust and fungal alpha-amylase ($r = 0.33$). Overall, a low proportion (39%) of bakery stores implemented various control measures to reduce dust exposures in the bakeries.

Conclusions: This study confirms that current exposure control strategies in supermarket bakery stores are inadequate in reducing dust exposures to protect the health of bakery workers.

Keywords: allergen; bakery; exposure assessment; exposure modeling; flour; fungal alpha-amylase; rye; wheat

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INTRODUCTION

Baker's asthma due to flour dust exposure in the work environment is one of the most commonly reported manifestations of occupational asthma in both industrialized and rapidly industrializing countries (Jeebhay and Quirce, 2007). Recent studies of the development of small- and medium-sized bakeries in South Africa over the past decade have demonstrated a dramatic rise in franchise (in-store) bakeries from 20% in 1995 to 44% in 2002. This has resulted in an increasing number of workers potentially at risk of developing baker's allergy and asthma. In a recent study of supermarket bakery workers, at least a quarter of workers were sensitized to cereal flour allergens and 13% has baker's asthma (Baatjies *et al.*, 2009). A fatal case of baker's asthma in a bakery assistant from a South African supermarket bakery has also been reported (Ehrlich, 1994).

Although exposure to inhalable dust, wheat, and fungal alpha-amylase allergens among workers in industrial, traditional, and supermarket bakeries is very well documented in several European and North American countries (Brant *et al.*, 2005; Elms *et al.*, 2005, 2006; Meijster *et al.*, 2009), no exposure data are available for bakeries in general and supermarkets in particular for rapidly industrializing countries, such as South Africa. Exposure data from studies in large industrial bakeries and traditional bakeries demonstrate that workers at the front end of the baking process (dough makers, bread formers, and bread bakers) have the highest average dust exposures (average inhalable dust exposures of 3–6 mg m⁻³) (Burdorf *et al.*, 1994; Nieuwenhuijsen *et al.*, 1994; Houba *et al.*, 1997). Furthermore, results from the only published study of bakeries in UK supermarkets showed that the mean (geometric) dust exposure concentrations for bakers were on average 1.2 mg m⁻³ (Brant *et al.*, 2005). Other more recent studies conducted in the UK also demonstrated that mixers/weighers/sievers had the highest median total dust and fungal alpha-amylase levels and suggesting that aside from job category, bakery size was also an important determinant of elevated exposure to flour dust allergens (Elms *et al.*, 2003a, 2005, 2006). These studies concluded that changes in the site of production of bread products from large scale industrial to small scale supermarket bakeries with the consequent burden of disease were important targets for proactive interventions aimed at reducing dust levels. It has been suggested that the use of appropriate knowledge and effective dust control measures, coupled with training and supervision, can substantially reduce flour dust exposure levels in bakeries. A sound evidence base for effective

interventions in bakeries is currently lacking. Meijster *et al.* (2008) have recently evaluated the potential of different control measures to reduce peak exposures. They concluded that more rigorous interventions than reduction measures nowadays regularly applied are needed to bring down exposure sufficiently (Meijster *et al.*, 2008, 2009).

This study is part of a larger intervention study entailing both exposure assessment and health outcome components. The study described in this paper aimed at assessing personal inhalable exposure to flour dust, wheat and rye allergens, and fungal alpha-amylase allergens in bakeries of a large supermarket chain store. Furthermore, an inventory of control measures currently used in these bakeries was also conducted. The results from the study will provide a baseline estimate of exposure and establish the basis for the intervention strategy to be implemented. The second major aim was to develop predictive exposure models based on the identified exposure determinants in the bakeries. It is envisaged that these models will be used to generate exposure predictions for individual participating in the health study to enable a more detailed study of exposure–response relationships for clinically relevant endpoints observed (Baatjies *et al.*, 2009).

METHODS

Study population

The study population consisted of workers from 18 bakeries from a large supermarket chain store in South Africa. Supermarket bakeries had an average workforce of 20 workers per bakery (range: 6–42) with an average production output of ~10 000 bakery units per week per bakery (range: 4360–18 346). Bakeries were stratified into small, medium, and large size based on the number of workers employed and the production output (bread, rolls, and cakes) of the bakery. The bakery size indices were derived using tertile values of the following variables as cut-off points—number of employees: ≤14, 15–21, and >21; and production output in units per week: ≤7504, 7505–10 868, and >10868. An equal number of bakeries were randomly selected from each stratum. Within each bakery, five main job titles could be distinguished: bread baker, bakery supervisor, bakery manager, confectioner, and counterhand (Table 1). From these selected bakeries, 109 workers (21%) were selected for sampling, while at the same time ensuring that all five job titles were adequately represented in each bakery. Using this sampling frame, all workers selected agreed to participate in the study.

Table 1. Description of jobs within supermarket bakeries in relation to main activities performed

Job title	Description
Bread baker	Mainly involved in tasks such as dough making; bread and roll production, which involves emptying bags of flour and other ingredients such as enzymes into a mixer; and weighing of ingredients, dusting of steel tables, and bread and rolls with flour.
Confectioner	Mainly involved with the baking and finishing (decorating) of cakes and pastries, including weighing of ingredients, preparing pastry dough, and operating dough processors.
Supervisor	Perform several tasks, including placing orders, supervising production, and frequently perform some tasks assigned to bakers.
Manager	Perform similar tasks to that of supervisors as well as training of workers, customer care, and frequently perform tasks of confectioners.
Counterhand	Serving customers, adequate stocking of the counter, and wrapping of products purchased by customers.

Walk through survey

Raw product inventory Prior to conducting the environmental sampling, an inventory of all ingredients used in all the bakeries was undertaken. Bulk samples of raw products were collected in sterile 50 ml Greiner centrifuge tubes and sent to Research Institute for Occupational Medicine (BGFA), in Germany, for analysis. The main aim of this inventory was to determine whether enzymes (fungal α -amylase and xylanase) were present in the flours and more specifically in the premixes used in these bakeries. The results were also to be used for identifying the panel of allergen extracts to be used for skin prick testing and allergen-specific IgE levels in the sera of workers in the epidemiological study.

Assessment of control measures A structured walk-through survey of all bakeries was also used to obtain detailed information with regard to work tasks, raw products used, and specific control measures implemented in relation to flour dust exposures in each bakery. The checklist included questions on the following parameters identified at each supermarket store: presence and type of ventilation system, use of personal protective equipment (3 M, FFP2 respirators), education and training activities, number of mixing tubs in each bakery, work practices during dough preparation (shaking of bags, enclosed mixing tubs, and use of oil versus flour for dough processing), and cleaning methods used in each bakery. Workers were observed throughout the shift and detailed information on tasks performed and specific work practices were recorded during personal environmental sampling. This process contributed towards the systematic prioritization of intervention measures and their subsequent evaluation in the next phase of the project.

Personal sampling measurements

Personal environmental sampling was performed on all selected study subjects on two consecutive

days. Full-shift samples were obtained on each participating worker using a PAS6 sampling head connected to a Gillian GilAir pump with constant-flow calibrated at 2 l min^{-1} . Teflon filters (Millipore; pore size $1.0 \mu\text{m}$, 25 mm diameter) mounted in the sampling head were used to collect the dust. Field blanks were included for each sampling day. Filters were weighed before and after sampling using a microbalance (Mettler Toledo AG245). Filters were acclimatized prior to weighing for 24 h in a room with controlled humidity (45%) and temperature (21°C) to ensure standard weighing conditions. The limit of detection (LOD) for the flour dust was 0.08 mg , calculated using the average weight difference of the blank filters plus three times the standard deviation. None of the samples collected had values below the LOD for total dust particulate.

Allergen concentration determination

After weighing for total dust particulate, the samples were prepared for immunological quantification by delaminating the filters and directly extracting them in 2.5 ml phosphate-buffer saline with 0.05% Tween-20, centrifuging 15 min at 1000 g , and storing the supernatant at -20°C (Bogdanovic *et al.*, 2006a). Wheat flour allergen concentrations were determined using an enzyme-linked immunosorbent assay inhibition technique with rabbit anti-wheat IgG4, and for samples below the detection limit, the sandwich enzyme immunoassay was used, as previously described (Bogdanovic *et al.*, 2006b). Fungal α -amylase allergens were measured using a sandwich enzyme immunoassay with monoclonal mouse antibodies for capture and affinity-purified polyclonal rabbit IgG antibodies for detection as described in Sander *et al.* (2007) and by Bogdanovic *et al.* (2006c).

Rye flour allergens were measured using a rabbit (NewZealand White) immunized with an allergenic rye seed extract (Sander *et al.*, 2005) and a two-sited

assay developed after Protein G purification of the coating antibodies and antigen affinity purification and biotinylation of the detection antibodies. Polymeric peroxidase-conjugated streptavidin (SA-poly-HRP80, RDI, Flanders, NJ, USA) and 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid (Sigma, Taufkirchen, Germany) as a substrate were used for measurement. Sample concentrations were read by interpolation of optical density values (OD₄₁₄ nm) on a four-parameter dose-response curve of the standard preparation, using Softmax Pro 4.7.1 from Molecular Devices (Sunnyvale, CA, USA). The assay was able to measure rye protein in a concentration range of 0.21–9.5 ng ml⁻¹. Each filter sample extract was measured in a dilution series of three 2-fold dilutions (first dilution at least 1:2). The mean coefficient of variation of these filter sample extract measurements was 7.8%.

Statistical analyses

All statistical analyses were performed using STATA version 8 and SAS version 9.1 (SAS 2002). Descriptive statistics were calculated stratified by job title. PROC UNIVARIATE procedure in SAS was used to explore the distribution of the exposure data. All exposure data followed a skewed distribution, requiring the exposure data to be log transformed prior to statistical analysis. Mixed effects models were used to evaluate the association between exposure to inhalable dust, wheat, rye, and fungal alpha-amylase allergens and covariates (e.g. job title, supermarket store size, tasks, and products), taking into account worker and supermarket store as random effects. PROC MIXED from SAS System Software Version 9.1 (SAS, 2002) was used for this analysis. We assumed a compound symmetry structure of the correlation matrix that any two repeated measurements of the same worker have equal correlation irrespective of the time interval between them. Mixed effects models were applied with and without the fixed effects to estimate the explained variance of the models produced. Variance components were estimated using the Restricted Maximum Likelihood method. Stepwise model building procedure was used to develop predictive models for inhalable dust, wheat, rye, and fungal alpha-amylase allergen concentrations with the final model only including covariates that were significant at the 10% level. Model improvement (increase in explained variance) was tested using the difference in -2-log likelihood ratio between the two models. If no additional variability was explained by adding more variables, expansion of the model was stopped. The percentage of the between-worker variance explained by the full

model in comparison to the empty models were calculated as follows: between-worker variance = $[(S^2_{\text{bw empty model}} - S^2_{\text{bw full model}}) / S^2_{\text{bw empty model}}] \times 100$.

RESULTS

Walk-through survey, product inventory, and control measures

The inventory of control measures in bakeries in most situations revealed a very low presence of control measures to reduce exposure to flour dust (Table 2). None of the bakeries made use of local exhaust ventilation; dough mixing tubs were not covered with lids resulting in dust becoming airborne during the dough mixing process, and vacuum cleaners were not used during cleaning operations. Furthermore, only 39% of bakery managers interviewed provided specific health and safety information to their workers on the precautions to reduce exposure to flour dust. Results of flour dust levels stratified by presence of control measures demonstrated no differences in average exposure levels when using process and behavioral control measures (divider oil, personal protective equipment, and training) (data not shown). However, structural controls such as physically separating departments were associated with markedly reduced levels of fungal alpha-amylase (0.30 versus 0.17 ng m⁻³, Wilcoxon rank-sum test $P = 0.125$).

Table 2. Uptake of control measures evaluated during walk-through survey of supermarket bakeries

Control measures	Uptake (%) (n = 31)
Structural/engineering controls	
Departments physically separated	2 (6)
Local exhaust ventilation system	0 (0)
Closure of mixing tubs:	
Partially closed	0 (0)
Totally closed	0 (0)
Process controls	
Use of divider oil instead of flour on dough table	1 (3)
Use of vacuum for cleaning	0 (0)
Surveillance of flour dust levels	0 (0)
Personal protective equipment	
Supply of appropriate personal respiratory protective equipment	11 (35)
Guidance on use of personal protective equipment	10 (32)
Information and training activities	
Information and training on flour dust	12 (39)

Analysis of bulk samples (two rye flour, eight wheat flour, and 16 premix products) for enzymes showed very low fungal alpha-amylase concentrations ($0.75\text{--}100\text{ ng mg}^{-1}$) in seven premix products and two rye products and was undetectable in remaining products. Xylanase levels were much lower ($<0.5\text{ ng ml}^{-1}$) and were only detected in a small proportion (3 of 16) of premixes and both rye flour products.

Personal exposure levels

A total of 211 full-shift personal samples were collected. Of the 109 workers sampled, 7 (6%) had one measurement and 102 (94%) had two repeated measurements. Bread bakers had the highest average flour dust particulate concentration [geometric mean (GM): 1.33 mg m^{-3}], double the exposure of confectioners and bakery supervisors, while the exposure of counterhands was half that of confectioners (GM: 0.28 mg m^{-3} ; Table 3). With respect to the distribution of wheat allergen levels, bakers (GM: $13.66\text{ }\mu\text{g m}^{-3}$) had twice as high exposures as confectioners (GM: $5.82\text{ }\mu\text{g m}^{-3}$) and confectioners five times higher than counterhands. Although similar patterns in levels of exposure in the different jobs were observed for rye allergen concentrations, these concentrations were generally half that of wheat allergen. The GM fungal alpha-amylase levels were relatively low (GM: 0.29 ng m^{-3}), with very minimal variation in exposure levels across the job categories and most samples (81%) being below the LOD.

Correlation analysis

A very strong correlation was observed between log-transformed inhalable dust particulate concentration and log-transformed wheat (Pearson $r = 0.84$, $P < 0.001$) and rye allergen concentrations (Pearson $r = 0.86$, $P < 0.001$) as well as between wheat and rye allergen concentrations (Pearson $r = 0.98$, $P < 0.001$; Fig. 1). However, the degree of correlation between inhalable dust and fungal alpha-amylase was much lower (Pearson $r = 0.33$, $P < 0.001$).

Mixed effects models

The results from the mixed effects models are presented in Table 4. The results reveal that significant predictors of elevated exposure to inhalable dust particulate, wheat, and rye allergen were job title, use of specific ingredients (flour), and working in a large bakery, while certain tasks such as confectionery work was negatively correlated with the exposure

Table 3. Personal inhalable particulate, wheat, rye, and fungal alpha-amylase allergens concentration levels in supermarket bakeries according to job title

Job title	k	n	Inhalable dust (mg m^{-3})				Wheat allergen ($\mu\text{g m}^{-3}$)				Rye allergen ($\mu\text{g m}^{-3}$)				Fungal alpha-amylase (ng m^{-3})			
			AM	GM	GSD	Range	AM	GM	GSD	Range	AM	GM	GSD	Range	AM	GM	GSD	Range
Bread baker	57	112	1.83	1.33	2.25	0.25–7.29	20.67	13.66	2.66	1.79–69.65	8.24	5.14	2.89	0.30–31.08	0.38	0.15	2.32	LOD–19.62
Confectioner	19	38	0.85	0.65	2.08	0.11–3.33	7.81	5.82	2.25	0.82–30.68	2.98	2.04	2.41	0.24–12.96	0.29	0.12	2.14	LOD–6.54
Baker supervisor	7	13	0.72	0.56	2.05	0.20–2.67	6.18	4.99	1.93	2.28–17.79	2.16	1.74	1.97	0.61–6.84	0.10	0.10	1.17	LOD–1.17
Bakery manager	7	13	0.72	0.51	2.34	0.12–2.48	7.93	3.41	4.01	0.32–40.28	2.52	1.99	4.06	0.09–9.32	0.14	0.12	1.58	LOD–0.51
Counterhand	19	35	0.35	0.28	1.89	0.11–1.96	2.80	1.16	4.81	0.002–29.86	0.98	0.39	4.57	LOD–10.92	0.12	0.11	1.40	LOD–0.64
Overall	109	211	2.21	1.80	1.92	0.11–7.29	13.71	6.71	4.09	0.002–69.65	5.36	2.42	4.30	LOD–31.08	0.29	0.13	2.08	LOD–19.62

AM: Arithmetic mean; GSD: geometric standard deviation; k: number of workers sampled in an exposure group; n: number of measurements in a group; LOD wheat: $0.001\text{ }\mu\text{g m}^{-3}$; LOD rye: $0.001\text{ }\mu\text{g m}^{-3}$; LOD fungal alpha-amylase: 0.083 ng m^{-3} ; number of measurements below LOD wheat: 0; rye: 1 (0.5%); fungal alpha-amylase: 169 (80%).

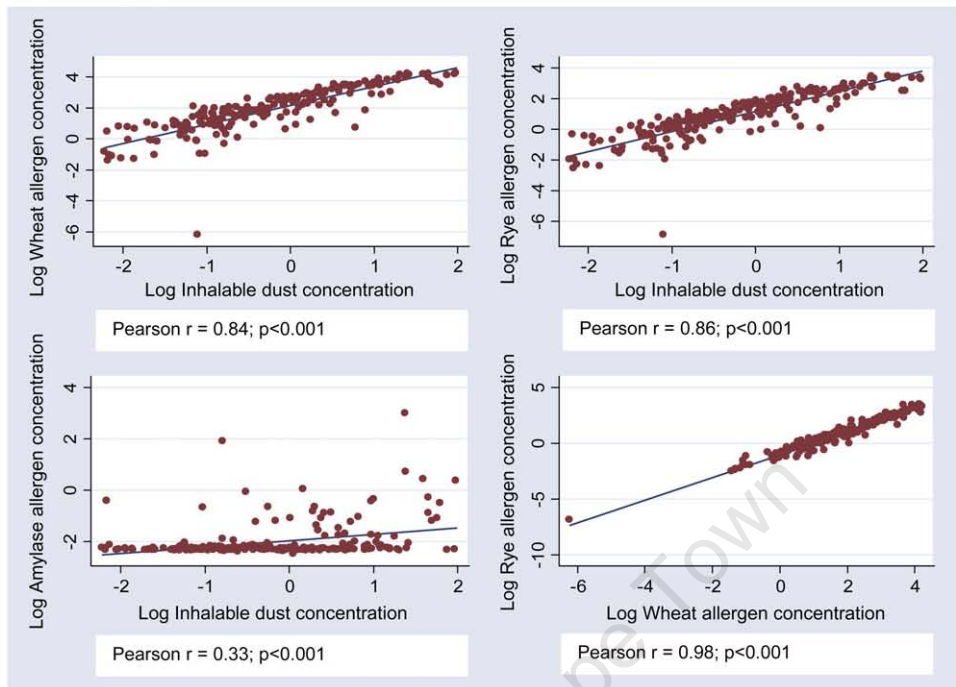


Fig. 1. Relationship between inhalable dust ($\ln \text{mg m}^{-3}$), wheat ($\ln \mu\text{g m}^{-3}$), rye ($\ln \mu\text{g m}^{-3}$), and fungal alpha-amylase ($\ln \text{ng m}^{-3}$) allergen concentration in supermarket bakeries: ($n = 211$).

Table 4. Estimates for variables in final mixed effects multivariate model of the log-transformed exposure to inhalable dust particulate and allergens (wheat, rye, and fungal alpha-amylase) in supermarket bakeries

Model variables (fixed effects)		Inhalable dust particulate		Wheat allergen		Rye allergen		Fungal alpha-amylase	
		β	P-value	β	P-value	β	P-value	β	P-value
Intercept ^a		-1.53	<0.001	-0.13	0.555	-1.26	<0.001	-2.21	<0.001
Job ^b	Bread baker	1.56	<0.001	2.54	<0.001	3.05	<0.001	—	
	Manager	1.33	<0.001	2.48	<0.001	3.04	<0.001	—	
	Confectioner	1.17	0.001	2.22	<0.001	2.80	<0.001	—	
	Supervisor	0.99	0.002	1.78	<0.001	2.20	<0.001	—	
Bakery ^c									
Tasks									
Tasks	Confectionery	-0.58	0.001	-1.01	<0.001	-1.28	<0.001	—	—
	Weighing ingredients ^d	—	—	—	—	—	—	0.21	0.057
Ingredients									
Ingredients	Flour use	0.27	0.091	0.37	0.084	—	—	—	—
	Premix product use	—	—	—	—	—	—	0.02	0.010
Var _{bw} (CI) ^e		0.19 (0.08–0.30)		0.28 (0.07–0.48)		0.36 (0.14–0.58) ^f			
Var _{ww} (CI) ^g		0.30 (0.23–0.41)		0.69 (0.53–0.93)		0.67 (0.52–0.90)		0.45 (0.37–0.56)	
Var _{bb} (CI) ^h		^r		^r		^f		0.04 (0.02–0.28)	

^aThe intercept gives the exposure level working as a counterhand in a small bakery without performing any of the tasks specified in the model and absence of flour use.

^bJob as counterhand is the reference group.

^cSmall bakeries are the reference group.

^dFixed effect not significant in final model.

^eVariance component between workers [confidence interval (CI)].

^fRandom effect not significant in model.

^gVariance component within workers (CI).

^hVariance component between bakeries (CI).

metrics. On the other hand, weighing tasks and use of premix products were associated with increased exposure to fungal alpha-amylase. Variability in exposure among supermarket bakery workers was moderately (40–52%) explained by models of flour dust particulate, wheat, and rye allergens and poor (8%) for fungal alpha-amylase (Table 4). A large component of the between-worker differences for dust particulate, wheat, and rye allergens were explained by the final models (71–80%; Table 5). The within subject (worker) variability was significant in all models for dust particulate, wheat, and rye allergens. The supermarket store random effect was significant only for fungal alpha-amylase, with 7% of the between bakery variability explained by the final model.

DISCUSSION

The results from this study demonstrate that bakers have the highest mean inhalable flour dust particulate, wheat, rye, and fungal alpha-amylase levels compared to other job titles. In the mixed effect models, job title, bakery size, and use of cereal flours were associated with significantly increased exposures, while tasks such as confectionery with decreased exposures. This is the first study to our knowledge documenting exposure to inhalable flour dust particulate and particularly wheat, rye, and fungal alpha-amylase allergens in the Southern African context and only one of the two studies conducted in supermarket bakeries globally. The findings will provide detailed baseline measurements for the intervention study currently being conducted.

Table 5. Variance components and confidence intervals (95% CI) of the log-transformed exposure to inhalable dust particulate and allergens (wheat, rye, and fungal alpha-amylase) in supermarket bakeries

Exposure variable	Exposure determinants	Between-worker variance	95% CI	Within-worker variance	95% CI	Reduction in between worker variance ^a
Dust	None	0.65	0.43–0.88	0.29	0.22–0.39	0
	Job	0.30	0.17–0.44	0.29	0.23–0.39	54
	Bakery size	0.62	0.41–0.84	0.29	0.22–0.39	5
	Tasks	0.64	0.42–0.86	0.29	0.23–0.39	3
	Ingredients	0.35	0.20–0.51	0.33	0.25–0.45	46
	Job + task	0.24	0.12–0.36	0.29	0.23–0.40	63
	Job + task + bakery size	0.21	0.10–0.32	0.29	0.23–0.39	68
	Job + task + bakery size + ingredients	0.19	0.08–0.30	0.30	0.23–0.41	71
Wheat	None	1.35	0.87–1.82	0.67	0.52–0.91	0
	Job	0.52	0.27–0.78	0.67	0.52–0.90	61
	Bakery size	1.33	0.86–1.80	0.67	0.52–0.91	1
	Tasks	1.33	0.86–1.80	0.68	0.52–0.91	2
	Ingredients	0.65	0.34–0.96	0.74	0.57–1.01	52
	Job + task	0.34	0.12–0.55	0.68	0.52–0.91	75
	Job + task + bakery size	0.31	0.10–0.52	0.67	0.52–0.90	77
	Job + task + bakery size + ingredients	0.28	0.07–0.48	0.69	0.53–0.93	80
Rye	None	1.52	1.00–2.04	0.67	0.52–0.91	0
	Job	0.62	0.33–0.90	0.67	0.52–0.90	60
	Bakery size	1.49	0.98–2.00	0.67	0.52–0.90	2
	Tasks	1.49	0.98–2.00	0.67	0.52–0.91	2
	Job + task	0.39	0.16–0.62	0.67	0.52–0.91	74
	Job + task + bakery size	0.36	0.14–0.57	0.67	0.52–0.90	77
Fungal alpha-amylase	None	0.05	0.12–0.31	0.49	0.40–0.60	0
	Tasks	0.05	0.02–0.28	0.46	0.38–0.57	–2
	Ingredients	0.04	0.02–0.29	0.46	0.38–0.56	8
	Task + ingredients	0.04	0.02–0.28	0.45	0.37–0.56	7

^aBetween-worker variance = $[(S^2_{bw} \text{ empty model} - S^2_{bw} \text{ full model}) / S^2_{bw} \text{ empty model}] \times 100$.

The mean inhalable dust particulate exposures of this group of supermarket bakery workers were lower than the levels reported by Bulat *et al.* (2004), Elms *et al.* (2005), and Meijster *et al.* (2007, 2009) among workers in industrial ($1.0\text{--}4.7\text{ mg m}^{-3}$) and traditional bakeries ($1.11\text{--}2.10\text{ mg m}^{-3}$) but comparable to levels reported by Brant *et al.* (2005) ($0.5\text{--}1.2\text{ mg m}^{-3}$) in a study of supermarket bakery workers in the UK (Brant *et al.*, 2005; Elms *et al.*, 2005; Meijster *et al.*, 2007, 2009). However, the GM wheat allergen exposures ($6.71\text{ }\mu\text{g m}^{-3}$) were comparable to recent studies in traditional bakeries ($7.4\text{ }\mu\text{g m}^{-3}$) but higher than levels observed in industrial bakeries ($3.6\text{ }\mu\text{g m}^{-3}$) (Meijster *et al.*, 2007). The mean fungal alpha-amylase levels were similar across most jobs in our study, most samples (81%) being below the LOD, and levels were generally much lower than levels reported by other studies ($0.40\text{--}1.7\text{ }\mu\text{g m}^{-3}$) (Elms *et al.*, 2006; Meijster *et al.*, 2007, 2009). These differences in enzyme levels were also observed in the analysis of bulk samples of products obtained from the bakeries under study, which demonstrated very low levels of fungal alpha-amylase, when compared to Dutch bakeries that generally contained much higher levels (Bogdanovic *et al.*, 2006). The results of the allergen exposure levels underscore the high prevalence of sensitization to wheat (26%) and rye (24%) flour when compared to the markedly low levels of sensitization to fungal alpha-amylase (4%) observed in the epidemiological study of workers employed in these bakeries (Baatjies *et al.*, 2009). Interestingly, although the mean dust exposure levels in the current study were similar to those reported by Brant *et al.* (2005) in UK bakeries (GM: 0.5 mg m^{-3}), the prevalence of sensitization to wheat was much lower (11%) in the latter study. It is unlikely that the atopy or smoking status of the subjects has played a major role as the prevalence of atopy in both study population was similar (41 versus 42%). Although the prevalence of smoking was higher in the South African study (47 versus 33%), it would appear that smoking does not have significant adjuvant effects in flour dust- (wheat, fungal alpha-amylase) exposed workers (Nielsen *et al.*, 2005).

While exposure to wheat and fungal alpha-amylase allergens among bakery workers has been well described, exposure to rye flour allergens has not been previously documented, and little is known about allergenic role of rye flour in baker's asthma. This is the first study to document occupational exposure to rye allergens among supermarket bakery workers as rye flour is increasingly being used in bread baking. An increasing number of studies, mainly case reports, have recently reported rye flour

allergens as an important cause of baker's asthma (Bensefa *et al.*, 2004; Ehrlich and Prescott, 2005; Letran *et al.*, 2008). Among these is a report of baker's asthma from a supermarket chain store of our study population, highlighting a greater clinical response to rye than wheat flour. These studies highlight a potentially emerging role of rye flour allergens in baker's asthma that merits further investigation.

In the mixed model analysis, aside from job status as a bread baker, large bakery size, specific tasks, and ingredients use were significant determinants of exposure. This is consistent with other studies, demonstrating bakery size, job, and tasks as significant predictors of dust particulate and wheat allergen exposures (Elms *et al.*, 2005; Peretz *et al.*, 2005). This observation is borne out in the epidemiological study that found that among those workers sensitized to wheat, 43% of workers worked in large bakeries (63 of 146), when compared to 24% working in small bakeries (35 of 146). An additional observation in our study was the use of premixed flour products that was significantly associated with higher levels of fungal alpha-amylase exposure. This finding is in agreement with previous studies suggesting that fungal alpha-amylase exposure is highly dependent on the mix of ingredients and the concentration of fungal alpha-amylase used (Meijster *et al.*, 2007). The bulk sample analysis in our study also demonstrated relatively higher fungal alpha-amylase concentrations ($0.75\text{--}100\text{ ng mg}^{-1}$) in premixed products compared to other raw products used. However, the concentration of xylanase was much lower ($<0.5\text{ ng ml}^{-1}$) and unlikely to be a major determinant of symptoms. Elms *et al.* (2003) have also shown that enzymes such as xylanase, cellulase, and hemicellulase cause sensitization in only 6% of bakery workers.

The exposure models developed for flour dust particulate and wheat allergen levels performed better in explaining total variability (48–52%) in exposure in this study of supermarket bakery workers when compared to Dutch traditional bakers (27–39%) (Meijster *et al.*, 2007). This may be explained in part by the fact that in the Dutch studies, different types of bakeries were included, whereas in the current study, the type of bakeries were similar, resulting in less exposure variability since the between-company differences are small (low contrast). However, studies by Burstyn *et al.* (1997, 1998) were able to explain up to 79% of total dust exposure variability since the investigators took into consideration various other determinants such as frequency and time spent on activities, which appeared to be an important source of day-to-day exposure variability.

Overall, exposure models in this study explained a significant proportion of between-worker variability for inhalable dust particulate and wheat and rye allergens (71–80%), which is comparable to the upper limit of the range of 56–78% reported by Peretz *et al.* (2005). However, the explained between-worker variability for fungal alpha-amylase was much lower (7%) and similar to a recent study in Dutch bakers explaining only 9% of the total exposure variability (Meijster *et al.*, 2007). This may in part be attributable to the low levels of fungal alpha-amylase found in bulk product samples obtained from these bakeries and the absence of a concentration gradient for fungal alpha-amylase across the various job titles in these bakeries.

The findings of this current study suggest that the measurement of inhalable flour dust particulate in personal samples may be a good surrogate of exposure to wheat and rye allergens due to the high correlation ($r = 0.84\text{--}0.86$) observed between these two parameters of exposure. This is an important factor to bear in mind with regard to hygiene monitoring, especially in resource-poor settings with limited access to advanced immunological assays. This information may be useful in measuring dust particulate levels when evaluating the impact of specific interventions to comply with legislative requirements. However, the degree of correlation between inhalable dust particulate and fungal alpha-amylase was much lower ($r = 0.33$), indicating that this does not hold for fungal alpha-amylase (Burstyn *et al.*, 1999).

In this study, an inventory of control measures in bakeries revealed a paucity of adequate measures (poor local exhaust ventilation systems, uncovered dough mixer tubs, and absence of vacuum cleaners) to reduce exposure to flour dust in most bakeries. However, the impact of structural controls was evident in that physically separate departments was associated with a 2-fold decrease in the fungal alpha-amylase exposures. This demonstrates that exposure to fungal alpha-amylase can be greatly reduced particularly among confectioners and workers not involved in bread baking by physically separating these processes in a bakery. Other studies evaluating the effectiveness of interventions in bakeries are limited. Burstyn *et al.* (1997) showed that the substitution of dusting with the use of divider oil in bread production was associated with lower exposures. Elms study in the UK found that although half of the bakeries were thought to have adequate control measures in place, activities such as dry sweeping and flour dusting by hand were common practices. The study concluded that knowledge of good work-

ing practices was limited and that with appropriate knowledge and use of good control practices, training, and supervision, exposure levels could be reduced (Elms *et al.*, 2005). Similarly, in the Netherlands, a lack of control measures to reduce exposure to flour dust was also observed in the flour sectors evaluated, and when control measures were present, their use was limited (Meijster *et al.*, 2007). Recently, a study investigating the long-term changes in flour dust exposure from 1985 to 2003 demonstrated that there was no significant downward temporal trend in flour dust exposures, despite initiatives to control dust exposure in bakeries (van Tongeren *et al.*, 2009). The study suggests that active involvement and commitment of government and industry is fundamental to reducing dust levels and the disease burden associated with high flour dust levels.

In conclusion, this study being the first exposure assessment undertaken in South Africa will provide an important baseline estimate of exposure in supermarket bakeries. The exposure models developed can now be used to generate exposure predictions for individual workers investigated during the baseline health study in order to study dose–response relationships for clinically relevant endpoints in baker's allergy. Despite the overwhelming evidence that workplace exposures to flour dust should be controlled, current prevention strategies in bakeries appear not to be very satisfactory. The intervention strategy of the larger study in South African supermarkets will be aimed at focusing interventions specifically linked to sources of high-risk exposures observed in this study. In this way, the detailed information gathered with regard to current control measures or lack thereof will be used to optimize the intervention strategy currently being implemented in these supermarket bakeries.

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CHAPTER 6

EXPOSURE- RESPONSE RELATIONSHIPS FOR WHEAT ALLERGEN EXPOSURE AND ASTHMA.

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CHAPTER 6

Exposure- response relationships for wheat allergen exposure and asthma.

Paper overview

In this paper exposure-response relationships are explored with specific reference to the allergens implicated and allergic disease endpoints. The nature of the exposure-response relationship for wheat allergen levels in relation to sensitisation, work-related symptoms and occupational asthma are described in detail. The possible role of IgG4 to wheat in this exposure-response relationship is also evaluated in order to explain the apparent non-linear pattern observed.

Contribution to the thesis and novelty

This article addresses the fourth objective. While few studies have investigated exposure-response relationships between wheat allergen exposure and allergic sensitisation, work-related symptoms and allergic rhinitis, objective data (bronchial hyper-responsiveness) for asthma endpoints has not been described prior to this study. Whilst exposure-response relationships have been described for wheat, the role of IgG4 to wheat in explaining the non-linear relationship has also not been investigated. This study explored the nature of exposure-response relationships for a range of clinically relevant allergic disease endpoints for bakery workers to investigate the role of IgG4 in these relationships.

Role of candidate

The candidate played a key role in the study design, data collection process, data management and advanced data analysis supported by Prof Dick Heederik. The candidate wrote the manuscript, incorporated

input from collaborators who critically reviewed the manuscript, and is responsible for the final submission of the manuscript.

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EXPOSURE-RESPONSE RELATIONSHIPS FOR WHEAT ALLERGEN EXPOSURE AND ASTHMA

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ABSTRACT

BACKGROUND: A few studies have investigated exposure-response relationships for sensitisation to wheat, work-related symptoms and wheat allergen exposure. IgG4 is suggested to protect against the development of allergic sensitisation. The main aim of this current study was to explore the nature of exposure-response relationships for a range of clinically relevant endpoints among bakery workers, and to investigate the role of IgG4 in these relationships.

METHODS: A cross-sectional study of 517 supermarket bakery workers in 31 bakeries used a questionnaire, serum specific IgE and IgG4 to wheat, and methacholine challenge testing. Exposure models were developed previously using job, bakery size, tasks and specific ingredients used. These models were used to predict average personal exposure to wheat allergens.

RESULTS:

The exposure-response relationships for average exposure followed a bell-shaped curve, with the prevalence of sensitisation, allergic symptoms and probable occupational asthma, increasing up to 10 - 15 $\mu\text{g}/\text{m}^3$ wheat allergen concentration after which they plateau off and decrease at higher exposure concentrations. This relationship was modified by atopic status. IgG4 levels were strongly exposure related: a clear increase in prevalence of higher IgG4 with increase in wheat allergen exposure was observed among those sensitised and non-sensitised to wheat, with IgG4 even more strongly associated with exposure than IgE to wheat.

CONCLUSION: The bell-shaped exposure response relationship in the current study is consistent with the findings of previous studies. IgG4 showed no protective effect for sensitisation, confirming the findings of previous studies, suggesting that the pattern is probably related to a healthy worker effect.

Keywords: exposure-response, wheat allergen, IgG4, sensitisation

Introduction

Exposure-response relationships have been previously described for alpha-amylase and wheat allergen exposures in relation to specific sensitization in bakery workers.^{1,2} Studies investigating the shape of the relationship between flour dust exposure and more specifically wheat allergen levels suggest that the dose-response relationship with sensitisation may be non-linear and level off or even decline at higher exposure levels.^{3,4,5} Furthermore, there have been no clear indications of an exposure level below which the risk for sensitization is zero or negligible. This bell-shaped response has also been observed in studies of exposure to rats in laboratory animal workers^{6,7} that have demonstrated an attenuation of specific IgE antibody response at high exposure levels.⁸

Some studies have suggested that the healthy worker effect is the likely explanation for the inverted relationship observed at high levels of exposure. Others have postulated that this may be due to the blocking effect or protective role of IgG4 antibodies.⁸ A “modified Th2 response”, mechanism has been used to explain the difference in the shape of exposure response relations in earlier studies of children for house dust mite when compared to those exposed to cat allergens and those receiving immunotherapy.^{9,10} The evidence from these studies suggests that IgG4 production is driven by increasing allergen exposure, resulting in a reduction of sensitisation in laboratory animal workers exposed to rats⁸, and mice¹¹, and children exposed to cats.⁹ Others have contested this view and showed that IgG4 antibodies to rat urinary allergen cannot explain the absence of a dose-

response relationship and does not protect against the development of respiratory allergy, but is merely considered a marker of exposure.^{12,13,14} This evidence is particularly strong because two of these studies are longitudinal studies. Aside from allergic sensitisation, there have been a few studies that have considered other endpoints such as symptoms, allergic rhinitis or baker's asthma in relation to wheat allergen exposure.¹⁵

This study is based on the results of a detailed health survey of South African bakery workers.¹⁶ The exposure estimates for wheat allergen used in the current study was based on baseline measurements of a subgroup of supermarket bakery workers previously reported¹⁷. The main aim of this current study is to explore the nature of exposure-response relationships for a range of clinically relevant endpoints such as allergic sensitisation, work-related allergic upper and lower airway symptoms and bronchial hyper-responsiveness among bakery workers.

METHODS

HEALTH OUTCOME ASSESSMENT

A cross-sectional study of 517 supermarket bakery workers employed in 31 bakeries used a European Community Respiratory Health Survey questionnaire, skin prick tests for atopy, and specific immunoglobulin E to flour dust allergens and methacholine challenge testing.¹⁶

Immunologic assessment

Serum specific IgE levels were available on 513 workers. Quantification of specific IgE antibodies to wheat (f4) was performed using CAP-FEIA (fluorescence enzyme immuno assay) according to the manufacturer's instructions (Thermofisher). An ImmunoCAP result of >0.35 kU/L was regarded as positive. For the purposes of our study, atopy was considered to be present if the SPT to one or more common aeroallergens was positive. The presence of atopy in workers who did not undergo SPTs ($n=10$) was defined by a positive Phadiatop test (ImmunoCAP 100 System; Phadia, Uppsala, Sweden).¹⁶

Specific IgG4 analyses

Serum analyses were performed for the quantitative measurement of wheat specific IgG4 antibodies using the UniCap assay procedure (ImmunoCap 100 System; Phadia, Uppsala, Sweden) according to the manufacturer's instructions. The fluorescence measured was transformed to concentrations with the use of a calibration curve. The calibrator ranged from 0 – 300 $\mu\text{g/l}$. The fluorescence response value is correlated with the specific IgG4

antibody concentration in the serum specimen. ImmunoCAP specific IgG control was included in the analyses for quality control. Values above the limit of quantitation (0.07 mgA/l or 70 µg/l) represent a progressive increase in the concentration of wheat specific IgG4 antibodies.

Spirometry

Spirometry was performed using the Jaeger Aerosol Provocation System (APS) Pro apparatus according to American Thoracic Society (ATS) guidelines.¹⁸ Methacholine challenge testing was performed on all workers by trained technologists according to an abbreviated protocol using the Medic Aid Pro Nebulizer dosimeter method as previously described.¹⁶⁶

Operational definitions of outcome variables

Upper and lower airway symptoms were considered to be work-related if they were reported to worsen during the work shift and improve when away from work.

1. *Probable Occupational asthma*: Defined as presence of non-specific bronchial hyper-responsiveness (NSBH); *and* sensitisation to wheat allergens
2. *Work-related allergic ocular-nasal symptoms*: Defined as presence of work-related ocular-nasal symptoms and sensitisation to wheat allergens
3. *Work-related allergic chest symptoms*: Defined as presence of work-related chest symptoms and sensitisation to wheat allergens

Sensitisation to wheat was defined as a positive SPT or elevated serum IgE to wheat.

EXPOSURE ASSESSMENT

Exposure metrics were derived from personal inhalable samples collected during the baseline survey.¹⁷ During exposure assessment, information on job title, supermarket store size, tasks, and products used were also collected to yield a total of 211 samples from 18 bakeries. Environmental samples were analysed for wheat allergens using the rabbit IgG inhibition EIA.¹⁹

Statistical analysis

Exposure models:

All statistical analyses were performed using STATA version 8 and SAS version 9.1 (SAS 2002). Since the exposure data followed a skewed distribution, the data was log transformed prior to statistical analysis. Mixed effects models were used to evaluate the association between exposure to wheat allergens and covariates previously described.¹⁷ The mixed model analysis of exposure determinants was conducted taking into account job title, tasks performed and other work characteristics. The information on work characteristics was obtained from the questionnaire interview and combined with the exposure models, to predict individuals average current exposures to occupational allergens for each worker in the past year. Ex-bakers were not included in the analysis of exposure-response relationships as it was not possible to assign a predicted exposure level to this group, as there were no

objective exposure measured since they were not currently working in the bakery. The exposure estimates were therefore reported on only 466 observations. The standardised questionnaire included designed for the investigation of asthma (respiratory symptoms, family history of allergy), was modified to include detailed questions relating to current and previous employment, degrees of exposure to flour dust, and tobacco smoke were included.

The following three exposure assessment approaches were considered according to methods employed in previous studies⁴: (i) measured exposure for each individual worker, (ii) estimated exposure based on the predictive model (which accounts for bakery size, job title, and tasks performed), and (iii) a combination of the previous two approaches, referred to as the variance-weighted estimator of exposure, based on measured and estimated exposure.

Modelling exposure–response relationships.

Nonparametric regression modelling (smoothing) was performed by using generalized additive models (proc gam) to explore and visualize the association between exposure and health for atopic and non-atopics separately. Generalized cross validation (GCV) was used to select the degrees of freedom for the smoothing component. In a number of cases, the curves in GAM showed large fluctuations that were not biologically plausible. In those cases the degrees of freedom were limited to a maximum of two. Estimates from the generalized additive models were exported to SigmaPlot

(v 9.0) to create smoothed spline plots for the different exposure–response relationships explored.

RESULTS

Health outcomes

A total of 517 workers were included in the analysis, on average 32 years old, and 51 were female. The prevalence of atopy, defined as a positive SPT to one or more common aeroallergens, was 42%. A total of 134 (26%), were sensitised to wheat, with 75% (100/134) having high levels of IgG4 (Table 1). A weak but significant correlation was observed for wheat IgE and wheat IgG4 (Spearman $r = 0.34$, $p < 0.001$). The prevalence of work-related ocular nasal symptoms (31%) was higher than work-related chest symptoms (17%), whilst wheat-related allergic symptoms were present in approximately half of these workers. These symptoms were more often reported by atopics compared to non-atopics for both work-related ocular nasal symptoms (OR: 2.2; $p < 0.001$) and work-related chest symptoms (OR: 1.6; $p = 0.060$). IgG4 levels were not significantly different for atopics and non-atopics. Self-reported work-related symptoms were associated with wheat specific IgE but not with IgG4 levels. Wheat specific IgG4 was significantly higher in workers with IgE sensitisation to wheat and in those with allergic work-related chest or ocular nasal symptoms (data not shown).

Exposure

Table 2 outlines the exposure levels for both average inhalable dust particulate and wheat allergen concentrations based on predicted exposure models. The average exposure was approximately 0.7 mg/m³ for inhalable dust particulate and 5 µg/m³ for wheat allergens (GM). The average duration of employment was 6 years.

Exposure-response relationships

Table 3 and Figures 1-4 present the results of exposure-response modelling. An increase in average current wheat exposure level was associated with a significant increase in the prevalence of wheat sensitisation (Figure 1) in a linear pattern. This relationship was more pronounced in atopics (p=0.047) compared to non-atopics (p=0.291).

Wheat allergen exposure was significantly associated with an increase in probable occupational asthma when using smoothing spline models (Table 3). Figure 2 illustrates that in atopic workers increased exposure to wheat allergens was associated with a higher prevalence of work-related allergic chest symptoms, work-related allergic ocular-nasal symptoms and probable occupational asthma (NSBH and sensitisation to wheat) in a dose-dependent manner. However, the prevalence of these symptoms only showed an increase up to 10 - 15 µg/m³ wheat allergen concentration and levelled off and decreased at higher exposure concentrations. The increased prevalence of upper respiratory symptoms appeared at a lower exposure than lower respiratory symptoms. The relationship between wheat allergen exposure,

sensitisation and symptoms in non-atopic workers however, showed insignificant associations. A further investigation of the exposure-response relationship for probable occupational asthma (NSBH and sensitisation to wheat) showed a flat relationship for non-sensitized individuals, but a steep increase for those with probable occupational asthma followed by a reduction in prevalence at exposure levels above $10 \mu\text{g}/\text{m}^3$.

To explain this bell-shaped relationship, the impact of IgG4 on the observed exposure-response relationship was investigated further. Table 4 demonstrates that an increase in wheat allergen concentration was significantly associated with IgG4 levels in wheat sensitised and non-sensitised workers, both for linear regression analysis and splines. Figure 3 clearly illustrated that IgG4 is strongly exposure related: a clear increase in prevalence of higher IgG4 with increase in wheat allergen exposure is seen. A similar exposure-relationship was observed among individuals sensitised and non-sensitised to wheat, with IgG4 more strongly exposure related than IgE to wheat.

Evaluating the relationship among those with probable occupational asthma showed that individuals with high IgG4 titres have a higher risk of having probable occupational asthma than those with low IgG4 (Figure 4a). This seems to indicate that IgG4 is merely a marker of exposure. A similar trend was observed for those with a high IgE/IgG4 ratio (Figure 4b).

In a simple logistic regression model for work-related chest and ocular-nasal symptoms, atopy, specific IgE and a high IgE/IgG4 ratio, were significantly associated with increased risk of symptoms. High IgG4 levels were also independently associated with a positive relationship with sensitisation (OR: 5.03; $p < 0.001$), ocular-nasal symptoms (OR: 1.61; $p = 0.013$), and not chest symptoms (OR: 1.29; $p = 0.273$).

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Table 1. Demographic and health outcome characteristics in supermarket bakery workers

Demographic and health outcomes	Overall (n=517)	Non-atopics (n=300)	Atopics (n=217)
Age (yrs)	32 ± 9	32 ± 9	30 ± 9
Gender (%F:M)	51:49	51:49	53:47
Atopy	217 (42%)	0 (0)	217 (100%)
<i>Specific IgE (n=513)</i>			
Wheat IgE *	134 (26%)	44 (15%)	90 (42%)
Wheat IgE (kU/L)	0.48 (4.46)	0.35 (3.14)	0.76 (5.89)
IgG4 (µg/l)	651.20 (6.02)	633.91(6.17)	675.50 (5.84)
IgE/IgG4 ratio	0.86 (1.25)	0.82 (1.18)	0.92 (1.30)
High IgG4**	239 (48%)	134 (46%)	105 (49%)
High IgE/IgG4***	255 (51%)	126 (43%)	129 (61%)
<i>Work-related symptoms (n=517)</i>			
Work-related ocular-nasal symptoms	162 (31%)	73 (24%)	89 (41%)
Work-related chest symptoms	86 (17%)	42 (14%)	44 (20%)
<i>Work-related allergic symptoms (n=513)</i>			
Work-related ocular-nasal symptoms	75 (15%)	23 (8%)	52 (24%)
Work-related chest symptoms	40 (8%)	15 (5%)	25 (12%)
Probable occupational asthma (n=453)	46 (10%)	11 (4%)	35 (19%)

Data are presented as % or Geometric mean and Geometric standard deviation; *Serum specific IgE>0.35 kU/l;

High IgG4 = calculated using the GM + 1SD as cut-off value for high versus low. *High IgE/IgG4 = calculated using the median of the ratio as a cut-off value

Work-related symptoms: Upper and lower airway symptoms were considered to be work-related if they were reported to worsen during the work shift and improve when away from work. *Allergic symptoms*: work-related symptoms, and sensitization (specific IgE to wheat); *Probable occupational asthma*: NSBH and sensitisation (specific IgE) to wheat

Table 2. Average inhalable dust and wheat allergen levels in supermarket bakery workers

Exposure characteristics	n	AM	GM	GSD	Range
Estimated Inhalable dust (mg/m ³)	466	0.87	0.69	2.01	0.12 – 5.42
Estimated wheat allergen (µg/m ³)	466	8.00	4.83	2.94	0.32 – 44.18

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Table 3. Association between wheat allergen exposure and clinical endpoints in supermarket bakery workers, stratified by atopic status in generalised additive models

Clinical endpoint	Average current exposure			
	Non-atopic Estimate	p-value	Atopic Estimate	p-value
Wheat sensitisation				
<i>Regression model (parametric part)</i>				
Intercept	-2.258	<0.001	-0.693	0.001
Linear component	0.038	0.052	0.045	0.023
<i>Smoothing model (nonparametric part)</i>				
Spline component	df = 1	0.291	df = 1	0.047
Work-related allergic ocular-nasal symptoms				
<i>Regression model (parametric part)</i>				
Intercept	-2.938	<0.001	-1.367	<0.001
Linear component	0.038	0.112	0.014	0.524
<i>Smoothing model (nonparametric part)</i>				
Spline component	df = 1	0.433	df = 1	0.215
Work-related allergic chest symptoms				
<i>Regression model (parametric part)</i>				
Intercept	-3.627	<0.001	-2.261	<0.001
Linear component	0.018	0.655	-0.009	0.845
<i>Smoothing model (nonparametric part)</i>				
Spline component	df = 1	0.135	df = 1	0.157
Probable occupational asthma				
<i>Regression model (parametric part)</i>				
Intercept	-3.380	<0.001	-1.436	<0.001
Linear component	0.007	0.896	-0.017	0.654
<i>Smoothing model (nonparametric part)</i>				
Spline component	df = 1	0.227	df = 1	0.045

Table 4. Association between wheat allergen exposure and clinical endpoints in supermarket bakery workers, stratified by IgG4 levels in generalised additive models

Clinical endpoint	Estimate	p-value
High IgG4		
<i>Regression model (parametric part)</i>		
Intercept	-0.550	<0.001
Linear component	0.052	<0.001
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.001
- Wheat sensitised group		
<i>Regression model (parametric part)</i>		
Intercept	0.463	0.164
Linear component	0.066	0.045
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.261
- Non-wheat sensitised group		
<i>Regression model (parametric part)</i>		
Intercept	-0.850	<0.001
Linear component	0.044	0.003
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.009
Probable occupational asthma		
<i>Regression model (parametric part)</i>		
Intercept	-2.126	<0.001
Linear component	-0.021	0.499
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.029
- High IgG4 group		
<i>Regression model (parametric part)</i>		
Intercept	-1.267	<0.001
Linear component	-0.062	0.135
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.188
- Low IgG4 group		
<i>Regression model (parametric part)</i>		
Intercept	-3.240	<0.001
Linear component	0.012	0.815
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.567

Table 4. Association between wheat allergen exposure and clinical endpoints in supermarket bakery workers, stratified by IgG4 levels in generalised additive models (continued)

Clinical endpoint	Estimate	p-value
Probable occupational asthma		
<i>Regression model (parametric part)</i>		
Intercept	-2.126	<0.001
Linear component	-0.021	0.499
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.030
- High IgE/IgG4 ratio		
<i>Regression model (parametric part)</i>		
Intercept	-0.940	0.003
Linear component	-0.076	0.055
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.187
- Low IgE/IgG4 ratio		
<i>Regression model (parametric part)</i>		
Intercept	-5.837	0.716
Linear component	0.119	0.860
<i>Smoothing model (nonparametric part)</i>		
Spline component	df = 1	0.380

High IgG4 = calculated using the GM + 1SD as cut-off value for high versus low.

High IgE/IgG4 = calculated using the median of the ratio as a cut-off value

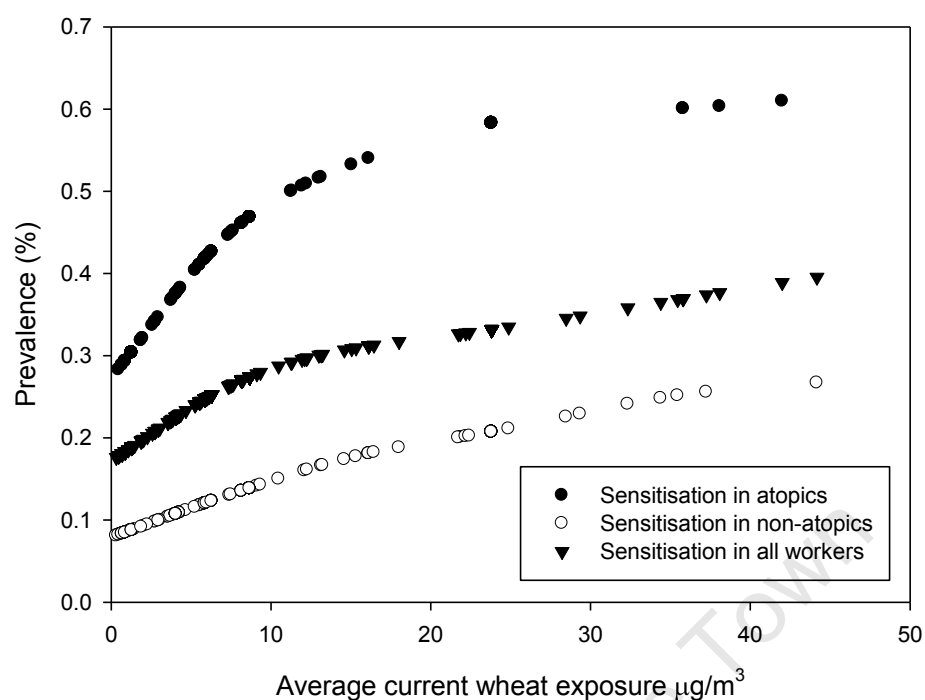


Figure 1. Relationship between wheat sensitisation and wheat allergen concentration among supermarket bakery workers, stratified by atopic status

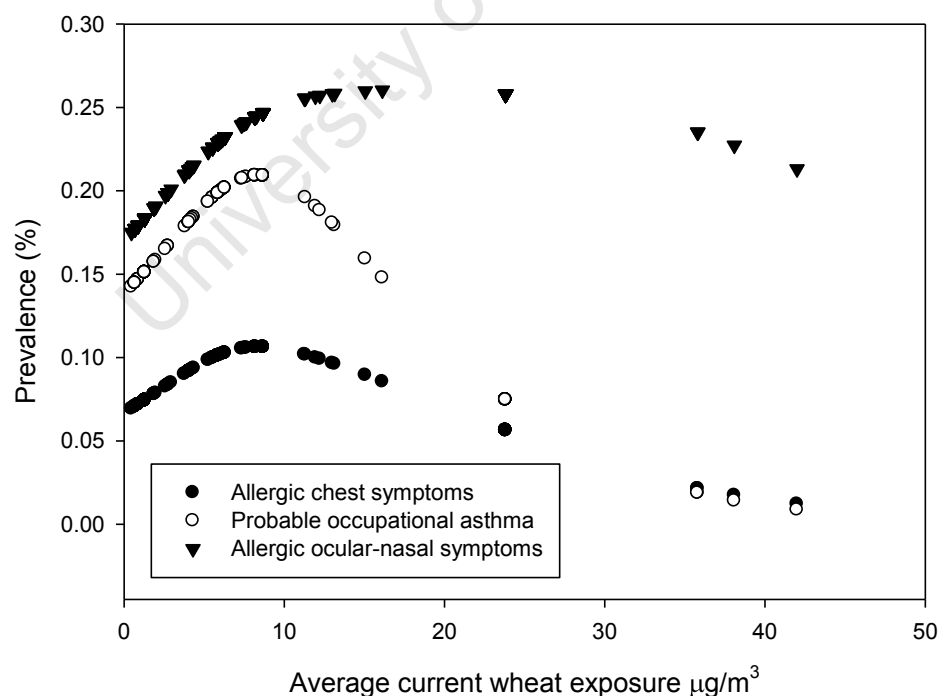


Figure 2a. Relationship between various clinical endpoints and wheat allergen concentration among atopic supermarket bakery workers

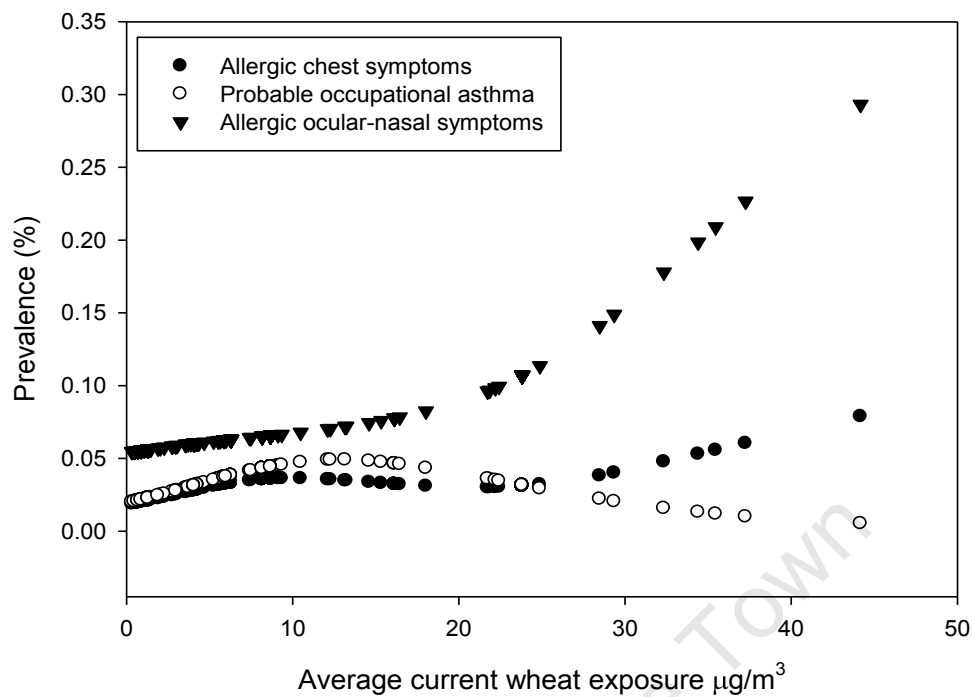


Figure 2b. Relationship between various clinical endpoints and wheat allergen concentration among non-atopic supermarket bakery workers

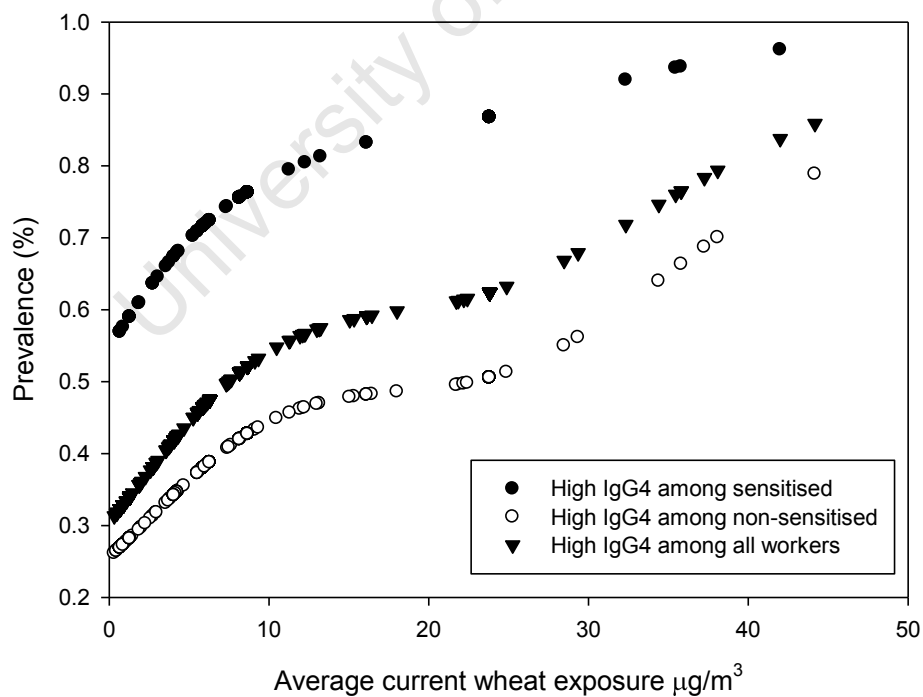


Figure 3. Relationship between IgG4 and wheat allergen concentration among supermarket bakery workers stratified by sensitisation

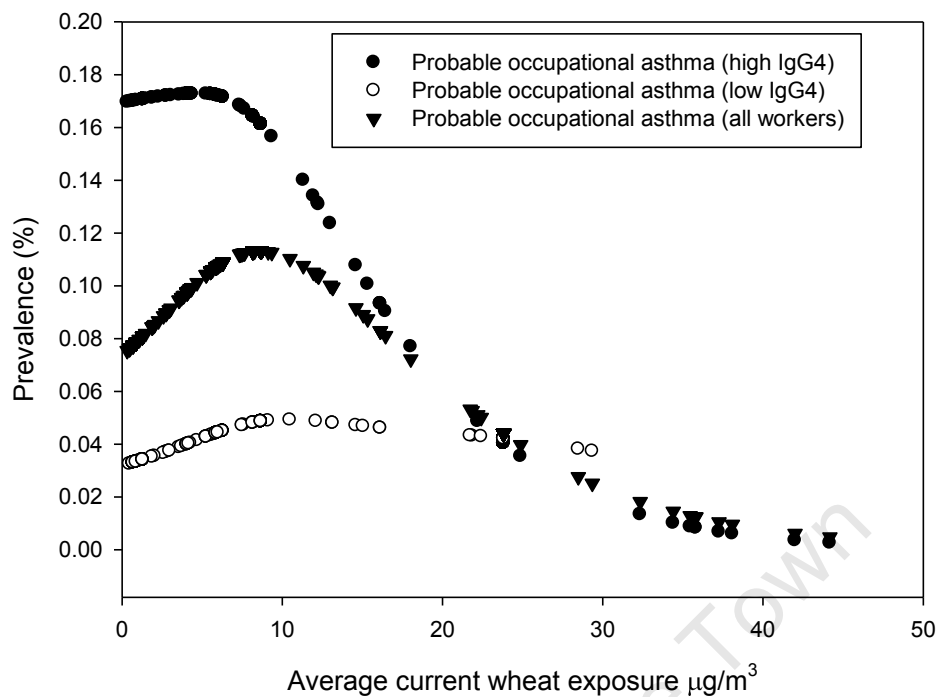


Figure 4a. Relationship between probable occupational asthma and wheat allergen concentration among supermarket bakery workers, stratified by level of IgG4

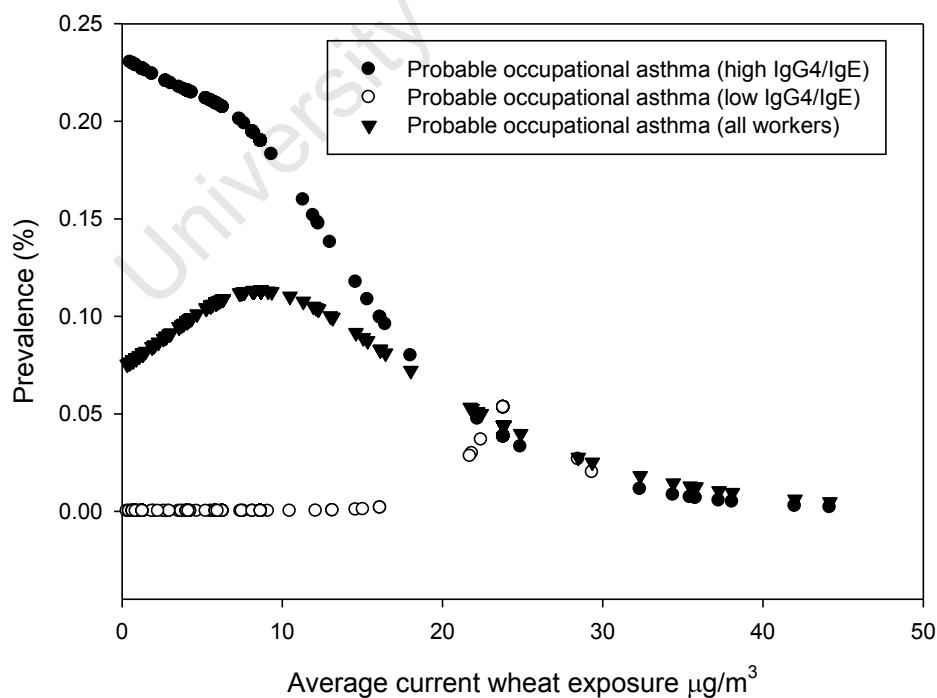


Figure 4a. Relationship between probable occupational asthma and wheat allergen concentration among supermarket bakery workers, stratified by IgG4/IgE ratio

DISCUSSION

The current study is one of few studies investigating the exposure-response relationship for occupational wheat allergen exposure in relation to sensitisation, symptoms and probable occupational asthma in bakers. While exposure-response relationships have been previously described for the former two outcomes, these studies were limited in that a critically relevant endpoint of baker's asthma was not modelled. The study is also the first detailed exploration of the role of IgG4 in explaining the non-linear exposure-response relationships observed in bakery workers.

The prevalence of probable occupational asthma (10%) in this study is at the upper end of the prevalence range (5-13%) of studies in industrial bakeries in which a similar definition of occupational asthma (bronchial hyper-responsiveness and sensitivity to flour) was used.^{20,21} However, a higher rate of sensitisation to wheat (26%) was found in the current study, when compared to earlier studies of industrial and supermarket bakeries (11-12%)^{22,23}, as well as in other studies of exposure-response relationships for wheat allergen exposures.⁵

In the current study a strong exposure-response relationship was demonstrated between wheat allergen exposure and the prevalence of wheat sensitisation, work-related allergic symptoms and probable occupational asthma. However, the exposure-response relationship was not linear, but an bell-shaped curve. These findings are consistent with previous studies, showing a similar bell-shape exposure-response relationship. In one of these

studies the prevalence of sensitization and symptoms increased with increasing wheat allergen concentrations up to $10\mu\text{g}/\text{m}^3$,³ as has been shown in the current study, whereas another study demonstrated increased sensitisation up to $25\mu\text{g}/\text{m}^3$ wheat allergen concentration,⁴ which was followed by declining risks at higher exposures. Bell shape curves for sensitization are not consistently observed. For instance, Houba et al² had no bell shape, while Peretz⁴ et al reported that the relationship for sensitization to wheat may be nonlinear but differs between industries. More recently, Jacobs et al⁵ also observed a bell shape exposure-response relationship. The differences in the observed exposure-response relationships could be ascribed to contextual differences between studies (exposure distribution, healthy worker effect, pre-employment selection, etc.). A detailed comparison shows that populations indeed differ in exposure distributions (higher in the flour millers and bakery product workers) and atopy (differences between bakery workers and flour workers) indicative of differences observed in the healthy worker effect.

The current study demonstrates an increase in sensitisation risk with increasing exposure, showing a linear relationship. However, a nonlinear bell shaped exposure relationship is observed for symptoms and probable occupational asthma (when NSBH is taken into account). A reanalysis of the earlier studies by Heederik et al³ also reported a bell shaped relationship when symptoms were taken into account. A possible explanation for these observations could be due to the fact that those with symptoms or NSBH cannot continue working at higher exposure levels, and therefore move to

lower exposed areas. However, longitudinal studies are required to allow for the direct observation of selective forces in this population. Furthermore, pooling of these various datasets in a pooled analysis may also contribute to a better understanding of these relationships.

The findings of this study demonstrated that an increase in wheat allergen concentration was significantly associated with IgG4 production in wheat sensitised as well as non-sensitised workers (in both regression and smoothing models), with IgG4 demonstrating even stronger exposure correlations than IgE to wheat. Furthermore, individuals with high IgG4 titres had a higher risk of having probable occupational asthma, and a similar trend was also observed for those with a high IgE/IgG4 ratio. These data suggest that increased IgG4 antibodies to wheat do not explain the bell-shaped exposure-response relationship between wheat allergen exposure and wheat allergy among bakers. This indicates that there is no evidence that IgG4 has a protective effect for becoming sensitized or developing allergic symptoms or occupational asthma in this study population. The relationship appears to be driven more by the IgE component of the equation.

These findings are consistent with previous studies, which also demonstrated that IgG4 does not protect against the development of sensitisation or allergy, but is considered to be merely a marker of exposure.^{12,13} In the first longitudinal study investigating the role of IgG4 in laboratory animal workers, titres of IgG4 showed a strong and positive dose response relationship with exposure to rat urinary allergens and were the highest in subjects who were

symptomatic and sensitized to rat allergens. The subsequent longitudinal study also found no protective effect of IgG4 against the development of IgE to rat allergens. This study further demonstrated that IgG4 responses develop prior to IgE responses and responses remained stable over time.¹³ Studies among bakery workers such as the one reported by Tiikkainen *et al*²⁴ suggested that the levels of IgG and IgG subclasses to wheat flour in bakers reflected exposure, but were not related to any specific clinical situation. Whilst, a study by Hur *et al*²⁵ also demonstrated that the levels of wheat-specific IgG1 and IgG4 antibodies were directly correlated with the levels of exposure to wheat and the concentration of wheat dust in the workplace.

Studies that have suggested a protective role for IgG4 have however also been reported. Jeal *et al*⁸ argued for the protective role on the basis that this could be explained by the fact that exposure to laboratory animals allergens did not only occur through inhalation but also from intradermal routes through bites and scratches. The same mechanism is also thought to explain the response in studies on domestic cat exposures,⁹ and beekeepers²⁶, but not bakers as it has been suggested that they are only exposed via the inhalation route. It is however possible that intradermal contact with wheat can also occur as they are known to have dermal symptoms and skin diseases related to allergen exposure. Furthermore, bakers also experience dermal trauma due to minor cuts and repeated hand washing. A recent study has demonstrated a possible exposure-response relationship between exposure to wheat allergens and work-related skin symptoms.²⁷

Conversely, other studies have suggested that high IgG4 antibodies may in fact be a risk factor for sensitisation^{11,12} as has been demonstrated in the current study in that high IgG4 was in fact associated with an increased risk for wheat sensitisation in this group of bakers. A longitudinal study among laboratory animal workers, also demonstrated that high levels of IgG4 predicted newly occurring sensitization and development of respiratory symptoms in atopic workers during follow-up.¹² This is consistent with a Korean study among bakery workers also demonstrating that the presence of specific IgG4 antibodies was associated with the occurrence of work-related symptoms.²⁵

The association between allergen-specific IgG4 and beneficial responses observed in relation to specific immunotherapy is still contested since it has been suggested that symptom relief could be induced by protective cytokines, such as IL-10, which is known to stimulate the production of IgG4 antibodies.²⁸ The effects of IL-10 and related cytokines are said to be important, since IL-10 interferes with the class switch, which affects both IgE and IgG4 production²⁹, and IL-10 increases IgG4 production and has been suggested to play a role in maintenance of tolerance.^{10,28,30,31,32} Furthermore, another study that investigated baker's asthma in two different populations (Spanish and French³³) concluded that the presence of higher levels of IgG4, IL10, and the diversity of sources of sensitization in French baker's patients may have helped them in reducing disease expression. However, since IL-10 levels were not measured in the current study, its role in explaining the patterns observed could not be explored further.

Some studies of gene-environment interactions have also suggested that exposure to occupational allergens such as endotoxin can significantly influence the exposure-response relationship.^{34,35,36} However, an experimental study in mice has demonstrated that endotoxin does not play a role in the inflammatory response to flour dust.³⁷

Our study instead suggests that the healthy worker effect, rather than tolerance at higher exposure levels is a more plausible explanation for the bell-shaped exposure-response relationship observed, but longitudinal observations are needed to confirm this explanation. Some evidence suggesting a healthy worker effect in the current study can be drawn from the observation that workers with OA were more likely to be supervisors/managers (OR = 4.0, $p=0.017$), rather than bakers (OR = 1.6, $p=0.312$) despite the fact that¹⁶ our environmental exposure studies¹⁷ have shown that bakers indeed had higher exposures to inhalable dust than supervisors/ managers. Furthermore, bakers with OA were also more likely to be transferred from their high exposure jobs to less exposed jobs (supervisors/managers) rather than those who worked in the least exposed jobs (counterhands). The baseline health study demonstrated that at least 6% of workers had to be transferred from their jobs due to them experiencing work-related chest symptoms.¹⁶

The healthy worker effect (HWE) may particularly affect epidemiological studies on work-related asthma in that while it is commonly appreciated that work in high risk exposure settings causes asthma, the asthma may have

substantial impact on work.^{38,39} To our knowledge this has not been studied in bakeries but recently, Dumas *et al*⁴⁰ have used marginal structural models (MSMs) to control for this healthy worker effect to assess the magnitude of bias due to the HWE. The study found that using MSM's associations increased for exposure to known asthmagens/sensitisers, and reached statistical significance for the relationship between exposure to low level of chemicals/allergens and asthma attacks, whilst these associations could not be demonstrated using standard conventional analytical techniques.

In conclusion, the bell-shaped exposure-response relationship in the current study is in agreement with the findings of previous studies. A strong exposure-response relationship between IgG4 and wheat allergen exposures, as well as for the IgE/IgG4 ratio, was found in sensitised and non-sensitised workers. These findings indicate that IgG4 has no protective effect on the development of sensitisation, and that this pattern is more readily explained by the healthy worker effect commonly observed in cross-sectional studies.

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CHAPTER 7

EFFECTIVENESS OF INTERVENTIONS TO REDUCE FLOUR DUST EXPOSURE IN SUPERMARKET BAKERIES.

University of Cape Town

CHAPTER 7

Effectiveness of interventions to reduce flour dust exposure in supermarket bakeries.

Paper overview

The final paper describes the group randomized intervention study conducted in these supermarket bakeries. It presents the details of the intervention and the follow-up flour dust exposure data in order to evaluate the effectiveness of different control measures that were designed to reduce airborne flour dust exposures.

Contribution to the thesis and novelty

This paper outlines the results in relation to the last objective of this research project. There is a dearth of evidence of exposure reduction strategies that use specifically designed interventions aimed at reducing the risk of baker's asthma. Even fewer studies are available that describe the effectiveness of interventions specifically in bakeries. This is the first study that incorporates both educational and technical engineering controls to reduce exposure to flour dust in bakeries.

Role of the candidate

The candidate designed the study, played a leading role in the development of the interventions together with engineers employed by the company and was responsible for data collection and data management. The candidate played a key role in conducting the advanced data analysis with support from Dr Tim Meijster. The candidate was solely responsible for drafting the manuscript and incorporating comments from collaborators, and is responsible for the final submission of the manuscript.

Publication status

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Appendices related to this paper

Appendix 9: Dust control manual

Appendix 10: Environmental data collection sheet

Appendix 11: Intervention checklist

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EFFECTIVENESS OF INTERVENTIONS TO REDUCE FLOUR DUST EXPOSURES IN SUPERMARKET BAKERIES IN SOUTH AFRICA

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ABSTRACT

RATIONALE: A recent study of supermarket bakery workers in South Africa, demonstrated that 25% of workers were sensitised to flour allergens and 13% had baker's asthma. Evidence on exposure reduction strategies using specifically designed interventions aimed at reducing the risk of baker's asthma is scarce.

OBJECTIVES: The aim of this study was to evaluate the effectiveness of different control measures to reduce airborne flour dust exposure using a randomized design.

METHODS: A group-randomised study design was used to assign 30 bakeries of a large supermarket chain store to two intervention groups and a control group. Full-shift environmental personal samples were used to characterise exposure to flour dust and wheat and rye allergens levels pre (n=176) and post (n=208) intervention.

RESULTS: The overall intervention effect revealed a 50% decrease in mean flour dust, wheat and rye allergen exposure. The reduction in exposure was highest for managers (67%) and bakers (47%), and lowest for counterhands (21%). For bakers, the greatest reduction in flour dust was associated with control measures like; the use of the mixer lid (67%), divider oil (63%) or focussed training (54%). However, the greatest reduction (80%) was observed when using a combination of all control measures.

CONCLUSION: A specially designed intervention strategy reduced both flour dust and allergen levels. Best results were observed when combining both engineering controls and training. Further studies will investigate the long term health impact of these interventions on reducing the disease burden among this group of bakers.

Keywords: exposure, flour dust, intervention, bakery workers

University of Cape Town

INTRODUCTION

The burden of occupational allergic respiratory disease due to airborne flour dust and bakery enzymes has been well documented (1) and is a major contributor to occupational allergic respiratory disease among food processing workers. In several earlier studies on bakery workers, 10-28% of workers were sensitized to cereal flour allergens, whilst the prevalence of baker's asthma was reported to be between 5-17%. (2,3,4,5,6,7) One third of workers with occupational asthma are unemployed up to six years after diagnosis.(8,9) Exposure-response studies have demonstrated a clear relationship between exposure to flour and bakery enzymes and specific sensitization or occupational asthma.(6,10,11,12) There is evidence indicating that substantial reduction in exposure will lead to a measurable reduction in disease burden.(13,14,15) While there have been some notable successes in reducing occupational asthma especially from latex in health care workers,(16) for most other allergens only few studies are available. Flour dust allergens levels show no decrease over the last decade.(17,18) Several dose-response studies indicate that exposure levels will need to be reduced by around 10-fold to have a significant impact on sensitisation and disease rates related to exposure to flour and enzymes.(12,19)

This highlights the need for effective interventions to reduce the incidence of occupational respiratory disease related to occupational flour dust exposure. (20) Prevention of occupational asthma related to work-sensitizing agents can be achieved by preventive measures such as substitution of the causal

agent(s) or reduction of the occupational exposures.(21) However, in the same publication it was explicitly noted that few studies exist on the effect of systematic interventions. While total avoidance is not possible in bakeries, exposure reduction is the preferred approach.

Well-designed intervention studies with detailed exposure characterisation to determine the effect of exposure reductions for occupational asthma are few.(22) Few studies are available that describe the effectiveness of interventions specifically in bakeries. This study presents the follow up exposure results of a larger intervention study incorporating both exposure assessment and health outcome components. The aim was to evaluate the effectiveness of interventions strategies introduced to in-store bakeries of supermarkets for improved flour dust control.

METHODS

Study design

The study employed a group-randomised design, particularly useful to evaluate interventions on a group level for example when workers are sharing a work site.(23) Bakeries were randomly assigned to an intervention as outlined in Figure 1. and were divided randomly into three equal groups taking into consideration the size of the bakery and number of workers in each bakery.

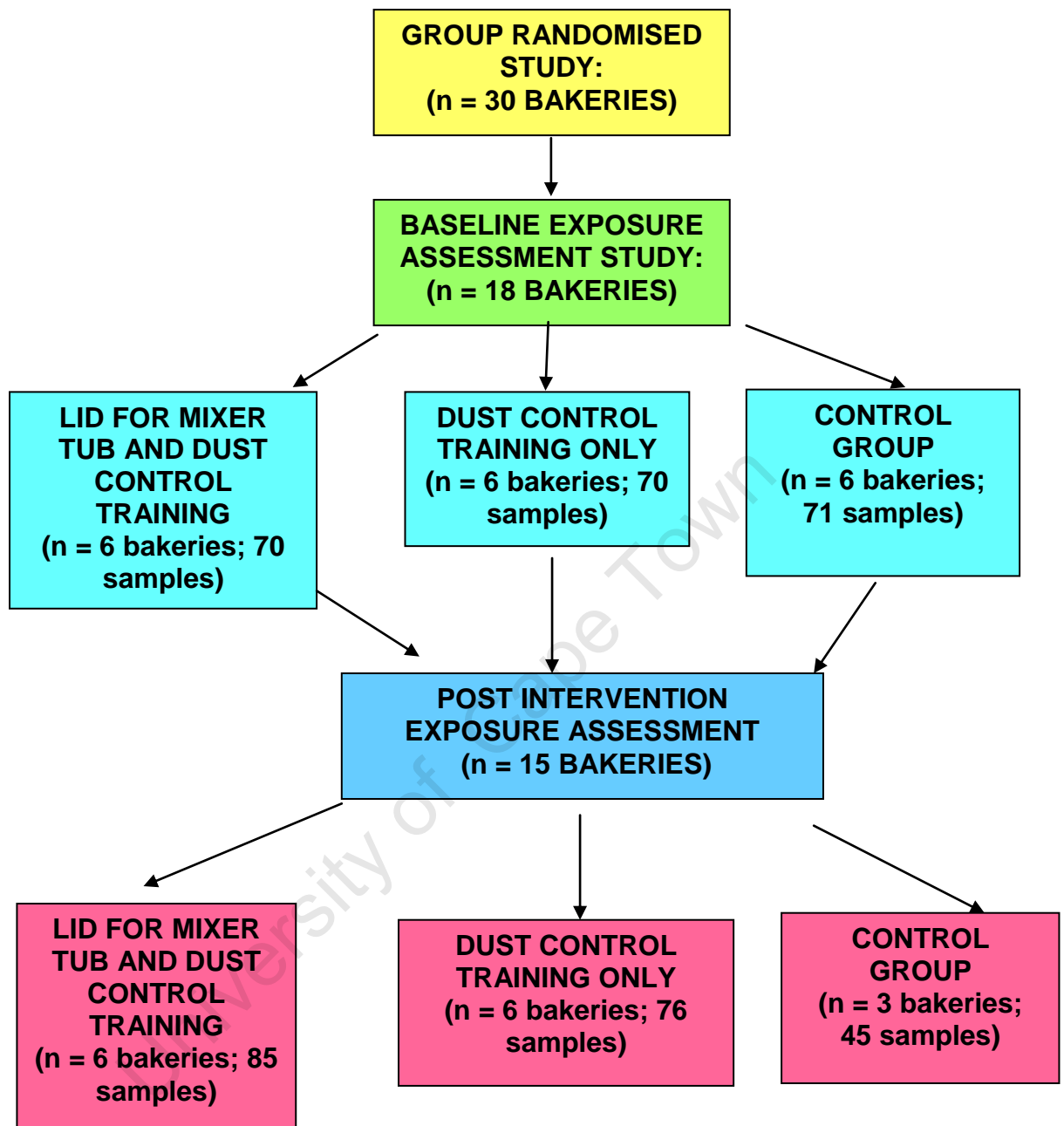


Figure 1. Flow diagram illustrating intervention study design and bakeries assessed pre-and post-intervention

Study Population

Environmental exposure of 18 bakeries that were previously assessed in the baseline exposure assessment study (24), were re-evaluated following implementation of the intervention. In this post intervention assessment three bakeries from the control group were lost to follow up for various reasons (e.g. closure) post-intervention, and consequently a lower number of samples were obtained from the control group.

a) Intervention development

Information obtained from the baseline study on determinants associated with high flour dust exposure and compliance with preventive measures were evaluated by the research team. This was accompanied by input from a multidisciplinary team of bakery workers, managers and engineers from the chain stores to inform the final intervention strategies that were developed and implemented. Information was available from the baseline study on presence and type of ventilation system; use of personal protective equipment; education and training activities; and number of mixing tubs in each bakery. Furthermore, various work practices were identified during dough preparation (shaking of bags, enclosure of mixing tubs, use of divider oil versus sprinkling with flour for dough processing), and cleaning of the bakery at individual level. Through focussed group discussions with stakeholders two specific intervention strategies were developed that incorporated engineering, administrative and behavioural components.

Intervention element 1: Redesigned lid for mixer tub

The evaluation indicated that use of mixer tubs was associated with high (peak) exposures (dumping of flour, mixing of products) (Figure 2a). Therefore, the first element of the intervention involved redesigning/refitting of the lid of the mixers tubs by introduction of a specialised lid with an inlet to prevent spillage of flour during dumping/emptying of flour from bags and when the mixer tub was operated at high speeds (Mc Adams South Africa), Figure 2b.



Figure 2a. Mixer tub with no lid, creating high dust exposures during dough mixing processes (adding flour to mixer)



Figure 2b. Redesigned mixer tub lid, with inlet to reduce flour dust exposure

Intervention element 2: Dust control training

The second element of the intervention focused on training of workers to improve awareness regarding the health risks associated with exposure to flour dust and following safer handling of flour and modified work procedures based on a similar approach developed for bakery workers in the Netherlands.^{1,2} The training covered the following elements:

- Work practices: Careful handling of bags when dumping/emptying into the mixer tub, during dough making (no shaking)
- Process controls: Using divider oils, rubbing flour or using a sieve for dusting dough table (instead of flour sprinkling) during dough processing
- Hygiene procedures: Using on the following options instead of dry sweeping with a normal bristle broom:
 - An industrial vacuum cleaner with a High Efficiency Particulate Air (HEPA) filter (Ghilbli AS 590, Supplier, Tennant), and wet methods
 - A rubber broom or microfiber mop
- Personal protective equipment: Using respirators (Model 8822 respirators, FFP2, supplier 3M) during short term dusty tasks such as mixing flour ingredients in a mixer tub without lid

The training program was directed at all workers with attention to specific tasks and work practices to reduce exposure to flour dust. A training video was developed to train all food handlers, illustrating sources of high flour dust

¹ <http://www.blijmetstofvrij.nl/images/2011-05/handboek-stofvrij.pdf>

² [http://www.oehru.uct.ac.za/docs/BAKERY%20DUST%20BOOKLET%20A5\(final\).pdf](http://www.oehru.uct.ac.za/docs/BAKERY%20DUST%20BOOKLET%20A5(final).pdf)

exposures and control measures to be followed to reduce these exposures. An intensive training programme for all managers and bakers in the stores was then undertaken by the research team. Training was conducted on-site in each bakery store. The training included a brief overview of the study, followed by the video presentation. That was followed by a discussion and a question and answer session. The training also included a demonstration on the correct use of the industrial vacuum cleaner.

b) Intervention implementation:

The intervention study undertaken had two interventions arms (Figure 1):

Group1, Lid for mixer tub and dust control training: The first group of 10 bakeries was assigned with a re-designed lid for the mixer tub in addition to being supplied with the flour dust control training manual accompanied by training workshops on its use. Each bakery was also provided with an industrial vacuum cleaner.

Group 2, Dust control training only: The second group of 10 bakeries was assigned only with the dust control training manual accompanied by training workshops on its use. Each bakery was also provided with an industrial vacuum cleaner.

Group 3, Control group: The third group was designated the comparison control group, which continued operating as usual with its bakery activities.

The interventions were implemented for at least one year. The investigators conducted unannounced random checks of all bakeries to assess the extent of adherence to the interventions. During these visits a checklist of compliance with intervention measures was completed. The findings of these inspections were communicated to employers and bakery managers to reinforce intervention adherence during this period of implementation.

Evaluation of intervention effectiveness

A post-intervention survey was conducted to evaluate the effectiveness of the different intervention strategies in relation to the control group (Figure 1). The post-intervention assessments were conducted at the end of the one year implementation period. Exposure measurements across all three groups were conducted on 15 of the 18 bakeries originally evaluated at baseline, since 3 bakeries were lost to follow up. Among these bakeries a total of 128 workers were selected for personal environmental sampling ensuring that all five job titles were adequately represented in each bakery. The sampling was performed on all study subjects on two consecutive days as was done in the baseline exposure assessment study.(26)

Flour dust and wheat allergen analysis and quantification

After weighing for inhalable flour dust particulate as described previously (24) the filters were prepared for immunological quantification. Extraction was done as described earlier (25) each sample was tested for wheat allergens by rabbit IgG inhibition EIA (26) on two separate occasions. The arithmetic

mean of the results was used as the wheat allergen concentration. Rye flour allergens were measured using a rabbit (New Zealand White) immunized with an allergenic rye seed extract (27) and a two-sited assay developed after Protein G purification of the coating antibodies and antigen-affinity purification and biotinylation of the detection antibodies.

Statistical analyses

All statistical analyses were performed using STATA version 11 and SAS version 9.1 (SAS 2002). Descriptive statistics were calculated stratified by job title and intervention group. PROC UNIVARIATE procedure in SAS was used to explore the distribution of the exposure data. All exposure data followed a skewed distribution, requiring the exposure data to be log transformed prior to statistical analysis. Mixed effects models were used to evaluate associations between specific controls and exposure measures in univariate analysis, using PROC MIXED from SAS System Software Version 9.1 (SAS, 2002). The models were used to evaluate the effect of the different control measures introduced both in separate models and the combined effect of all measures observed during the exposure assessment. Analyses were performed overall, for example for training, and per job where relevant and compound symmetric correlation was assumed for repeated measurements in the same subject. Stepwise model building procedure was also used to identify determinants of flour dust reduction for inhalable flour dust and flour dust allergens.

RESULTS

Table 1 provides descriptive data for the exposure assessment both pre- and post-intervention. The analysis was only conducted on groups for which we had exposure data pre-and post-intervention, due to a few bakeries in the control groups being lost to follow-up. A comparison of the overall intervention effect (baseline versus post intervention), revealed a 50% decrease in geometric mean (GM) inhalable dust exposures, 56% for wheat allergen, and 61% for rye allergen levels (Table 1). The overall intervention effect was similar across the two intervention groups. Surprisingly, the control group also showed a substantial reduction in average exposure concentration, however, to a lesser extent for allergen levels. However, the reduction (57-67%) in wheat allergen levels among the intervention groups were almost double that of the control group (19-38%). As a result, no significant difference in reduction was observed in intervention groups when compared to the control group. The reduction in exposure in controls seemed associated to uptake of control measures following the introduction of the interventions (Table 2). For example, bakers in the control group bakeries started using divider oil more frequently instead of flour (71% vs 58%), and shook bags less frequently when opening them (21% versus 67%). The reasons for the introduction of intervention measures in the control group seemed associated with transfer of managers from the intervention group bakeries to the non-intervention group bakeries. After transfer they introduced some of the new work practices in the control bakeries. As a result, we could not analyse the effects of interventions by comparing

differences in trends in exposure between the different treatment groups and the controls. Alternatively, we explored the effect of changes in control measures on changes in exposure over time, across the different intervention groups.

The majority of workers in the intervention groups received training as described previously (78-88%). Those who did not attend the training were either on vacation, sick or not available. However, half (51%) of the workers in group one were non-compliant and did not use the lid according to the guidelines, and none of the intervention groups used the industrial vacuum cleaner on a regular basis.

A comparison of the reduction in exposure levels by job title is outlined in Table 3. The average percentage reduction in flour dust particulate (21-67%), wheat (33-67%) and rye allergen levels (42-76%) were highest for managers (54-76%), with bakers having an average reduction in exposure levels of 45-48%, whilst the least reduction was observed for counterhands. The analysis was adjusted for the potential imbalanced job title distribution over groups, and showed no significant differences in the mean levels after adjusting for intervention group.

Table 4 outlines the results of the identified control measures that were evaluated, corrected for intervention group. The effect of the use of the lid was estimated in the following groups: 1) for bakers in post intervention group, who had lids and used it compared to bakers who did not use the lid,

but had a lid (n=43); 2) for bakers who used lids compared to all other bakers who did not use a lid (n=186); 3) for bakers who had lids and used it to all bakers who did not have lids, and excluding those who had lids but did not use it (n=164). The effect of divider oil was also analysed in two ways: 1) bakers who used divider oil compared to bakers who did not use divider oil (n=186); 2) bakers who used divider oil post intervention compared to bakers who did not use divider oil and excluding those who used divider oil pre-intervention (n=139). Correcting the estimates for the possible intervention group effect, did not significantly impact on the beta estimates, and the group variable was not significant in any of the models, indicating that control measures are causally associated to changes in exposure. The use of a mixing tub with a lid ($\beta=-1.10$; 67%), use divider oil instead of flour ($\beta=-0.99$; 63%) and rubbing the dough table ($\beta=-0.79$; 55%) with flour, gentle handling and opening of bags ($\beta=-0.89$; 59%) and low dusting practices ($\beta=-0.79$; 55%) were all associated with significantly lower flour dust and allergen exposures. A composite variable that reflected the impact of the five combined interventions (a positive response to all of the following interventions: use of divider oil, gentle handling and opening of flour bags, low dusting of dough tables, rubbing the dough table with flour, correct use of lid on mixing tubs) was developed. The results demonstrate that the greatest reduction in flour dust (80%) and wheat allergen (72%) levels was achieved if workers employed a combination of all five control measures. A lower reduction in flour dust (48%) and wheat allergen (61%) was obtained if the lid was not installed and used on the mixer tub, and slightly lower reductions in flour dust (45%) and wheat allergen (41%) when using any one of the

interventions. The results for rye allergens were essentially similar to the findings for wheat allergens and therefore not presented.

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Table 1. Comparison of changes in flour dust exposure particulate, wheat and rye allergen exposures pre- and post intervention in supermarket bakeries

	BASELINE					POST-INTERVENTION					AVERAGE CHANGE (%)
	n	AM	GM	GSD	Range	n	AM	GM	GSD	Range	
Inhalable flour dust (mg/m ³)											
TOTAL OVERALL	176	1.35	0.86	2.64	0.11 – 7.29	208	0.64	0.43	2.56	0.01 – 4.07	-50%
LID AND TRAINING	70	1.25	0.85	2.44	0.12 – 6.57	85	0.61	0.39	2.77	0.01 – 3.27	-54%
TRAINING ONLY	70	1.58	0.95	2.89	0.11 – 7.29	78	0.70	0.47	2.43	0.07 – 4.07	-51%
CONTROL GROUP	36	1.11	0.74	2.54	0.11 – 5.25	45	0.62	0.44	2.41	0.06 – 2.55	-41%
Wheat allergen (µg/m ³)											
TOTAL OVERALL	176	14.49	7.07	4.21	0.00 – 69.64	206	7.04	3.12	4.17	0.05 – 48.56	-56%
LID AND TRAINING	70	14.60	7.25	4.74	0.00 – 62.75	85	6.08	3.11	3.81	0.06 – 35.28	-57%
TRAINING ONLY	70	17.21	8.52	3.96	0.24 – 69.64	76	7.80	2.80	5.07	0.06 – 48.56	-67%
CONTROL GROUP	36	8.98	4.70	3.51	0.34 – 51.90	45	7.57	3.79	3.45	0.51 – 42.25	-19%
Rye allergen (µg/m ³)											
TOTAL OVERALL	176	5.67	2.57	4.43	0.00 – 31.08	206	2.42	1.01	4.17	0.03 – 29.37	-61%
LID AND TRAINING	70	5.23	2.43	4.86	0.00 – 26.90	85	2.16	0.90	4.14	0.03 – 29.37	-63%
TRAINING ONLY	70	7.02	3.13	4.39	0.07 – 31.08	76	2.71	1.04	4.50	0.03 – 15.97	-67%
CONTROL GROUP	36	3.87	1.96	3.64	0.13 – 26.01	45	2.42	1.21	3.72	0.06 – 10.20	-38%

n: number of measurements in a group; AM: Arithmetic mean; GM: Geometric mean; GSD: geometric standard deviation

Table 2. Inventory of control measures and level of compliance among bakers in all study groups pre- and post-implementation of intervention in supermarket bakeries

Control measures	Adherence prevalence (%)					
	Group 1		Group 2		Group 3	
	Pre- (n=6)	Post (n=6)	Pre- (n=6)	Post (n=6)	Pre- (n=6)	Post (n=3)
Training conducted	-	78	-	88	n/a	n/a
Lid installed onto mixer tubs	n/a	100	n/a	n/a	n/a	n/a
Lid used by bakers	n/a	49	n/a	n/a	n/a	n/a
Low dusting of dough tables	0	86	0	58	0	71
Rubbing of dough table with flour	-	67	-	42	-	43
Divider oil for rubbing dough tables	21	58	-	45	-	71
Gentle handling and opening of flour bags	0	33	0	32	0	79
Vacuum used	-	-	-	-	-	-
Group 1 = Lid for mixer tub and flour dust control training						
Group 2 = Flour dust control training only						
Group 3 = Control group						

Table 3. Personal inhalable flour dust particulate, wheat and rye allergen exposures pre- and post intervention in supermarket bakeries stratified by job title

Job title	k	n	AM	BASELINE			Range	k	n	POST INTERVENTION				Range	AVERAGE CHANGE (%)
				GM	GSD					AM	GM	GM*	GSD		
Inhalable flour dust (mg/m ³)															
Bread baker	49	98	1.89	1.39	2.23	0.25 – 7.29	52	88	0.97	0.74	0.79	2.16	0.04 – 4.07	-47%	
Confectioner	14	28	0.94	0.73	1.95	0.29 – 3.33	34	57	0.51	0.41	0.43	2.06	0.05 – 1.68	-44%	
Baker Supervisor	5	9	0.82	0.61	2.24	0.20 – 2.67	7	11	0.36	0.23	0.23	3.43	0.01 – 1.01	-62%	
Bakery Manager	5	9	0.87	0.60	2.58	0.12 – 2.47	5	8	0.35	0.20	0.21	2.80	0.05 – 1.56	-67%	
Counterhand	17	32	0.36	0.28	1.91	0.11 – 1.95	30	44	0.29	0.22	0.23	2.09	0.03 – 1.23	-21%	
Overall	90	176	1.35	0.86	2.64	0.11 – 7.29	128	208	0.64	0.43	0.38	2.56	0.01 – 4.07	-50%	
Wheat allergen (µg/m ³)															
Bread baker	49	98	21.06	13.66	2.76	1.79 – 69.64	52	87	11.84	7.51	10.03	2.89	0.18 – 48.56	-45%	
Confectioner	14	28	8.48	6.76	1.98	1.71 – 30.66	34	56	4.85	2.73	3.50	3.51	0.06 – 20.49	-60%	
Baker Supervisor	5	9	6.53	5.34	1.90	2.33 – 17.80	7	11	4.16	1.77	2.49	3.81	0.35 – 18.40	-67%	
Bakery Manager	5	9	10.72	4.91	4.55	0.32 – 40.28	5	8	5.48	2.25	2.76	4.12	0.54 – 20.08	-54%	
Counterhand	17	32	2.91	1.18	4.98	0.00 – 29.85	30	44	1.32	0.79	1.07	2.86	0.06 – 10.63	-33%	
Overall	90	176	14.49	7.07	4.21	0.00 – 69.64	128	206	7.04	3.12	2.82	4.17	0.06 – 48.56	-56%	
Rye allergen (µg/m ³)															
Bread baker	49	98	8.41	5.17	2.96	0.30 – 31.08	52	87	4.27	2.67	3.63	2.70	0.21 – 29.37	-48%	
Confectioner	14	28	3.17	2.31	2.19	0.53 – 12.96	34	56	1.54	0.91	1.18	3.03	0.09 – 6.48	-61%	
Baker Supervisor	5	9	2.33	1.94	1.83	0.88 – 6.84	7	11	1.22	0.60	0.80	3.60	0.13 – 3.77	-69%	
Bakery Manager	5	9	3.37	1.75	4.50	0.10 – 9.32	5	8	1.62	0.42	0.49	5.86	0.03 – 8.80	-76%	
Counterhand	17	32	1.03	0.40	4.75	0.00 – 10.92	30	44	0.36	0.23	0.30	2.51	0.03 – 2.88	-42%	
Overall	90	176	5.67	2.57	4.43	0.00 – 31.08	128	206	2.42	1.01	0.78	4.17	0.03 – 29.37	-61%	

k: number of workers sampled in an exposure group; *n*: number of measurements in a group; AM: Arithmetic mean; GM: Geometric mean; GM*: corrected for intervention group; GSD: geometric standard deviation

Table 4. Specific determinants of flour dust control reduction measures in the mixed effects model of inhalable flour dust particulate and wheat allergen concentrations among bakers in supermarket bakeries

Model variables	Inhalable flour dust particulate (ln) mg/m ³				Wheat allergen (ln) µg/m ³			
	N	β	p-value	% change	N	β	p-value	% change
Fixed effects of individual interventions								
Lid used correctly by bakers	164	-1.10	<0.001	-67	163	-0.82	0.029	-56
Training instruction received	311	-0.77	<0.001	-54	309	-0.99	<0.001	-63
Divider oil for rubbing work dough tables	139	-0.99	<0.001	-63	138	-0.84	<0.001	-57
Rubbing of dough table with flour	146	-0.79	<0.001	-55	145	-0.73	0.001	-52
Low dusting of tables	163	-0.79	<0.001	-55	162	-0.75	<0.001	-53
Gentle handling and opening of bags	133	-0.89	<0.001	-59	133	-0.70	0.007	-50
Combination of interventions								
No intervention	103	0	-	-	103	0	-	-
Applying all 5 methods of control	10	-1.61	0.029	-80	10	-1.26	0.074	-72
Applying only 2 methods of control	7	-0.65	0.208	-48	7	-0.94	0.190	-61
Applying any one method of control	66	-0.60	0.057	-45	66	-0.53	0.126	-41

DISCUSSION

To our knowledge this is the first attempt to introduce a well-designed intervention study in bakeries, evaluating the impact of localised specific intervention strategies. The study demonstrated a significant overall reduction in inhalable flour dust particulate (50%), wheat (56%) and rye (61%) allergen exposure in bakeries from baseline. Stratifying the data for different jobs changed the overall effect by less than 5%, suggesting no appreciable sampling effect. This is also the first study to demonstrate such a substantial reduction in exposure to flour dust and allergens in the workplace environment.

Studies, designed to evaluate changes in exposure across time are also limited. In one of the most well described studies in the wood processing industry a group randomised trial was used in which the intervention group received extensive intervention (written recommendations, technical assistance, and worker training) while the control group only received written recommendation.(23) However, a lower than expected reduction (26%) was observed. These findings were ascribed to a short observation period, lack of intensive interventions, and possible contamination among the control businesses through encounters with owners and workers from intervention businesses. A pragmatic intervention study in the Dutch bakery industry, also found a small (2%) reduction in average exposure to flour dust and allergens per year following large scale dissemination of an educational program on

exposure control, while other studies have shown reductions mainly at task level.(18,28)

In the current study, the intervention effect was similar across the two intervention groups, with the control group also showing a substantial reduction in average exposure concentration. The changes in work practices observed in the control group, and the consequent reduction in exposures in this group are indicative of a dilution effect and/or contamination among bakeries. This is in all probability due to the reported movement of managers between bakeries (from intervention group bakeries to control group bakeries), also a result of promotion or job rotation; a greater awareness of risks of flour dust as a result of being in the study; and to a lesser extent encounters of control group workers with workers from intervention bakeries during the period of the intervention. This was evident in the evaluation of the changes and uptake of control measures following the introduction of the interventions is out. Notably, changes in work practices were also observed in the control group. For example, bakers in the control group bakeries started using divider oil more frequently instead of flour (71% versus 58%), and shook bags less frequently when opening them (21% versus 67%). Overall, it is also probable that participation in such a study may have led to the adoption of safer work practices even in the absence of targeted interventions to reduce exposure.

In this study, the change across job categories showed an average reduction in exposure among bakers of 45%, whilst a much greater reduction was observed among managers in these bakeries. These changes could be attributed to the reduced active involvement of managers in the work processes over time due to increased administrative responsibilities, resulting in less time being spent in the bakery section of the supermarket. Although the average reduction in exposures differed by job title, the interventions were mainly directed at bread bakers, since this group of workers were involved in tasks with highest flour dust exposure.

Bakeries that substituted flour with divider oil showed clear reductions in flour dust exposures. Studies by Burstyn et al (29,30) also showed a 28-fold decrease in flour dust exposure when substituting dusting flour with divider oil, whilst Meijster et al (31) found a more modest reduction in exposure when substitutes like divider oil and dust-free flour were used. However, in the current study process divider oil in the presence of other exposure determinants was not found to be a significant exposure determinant contrary to the other studies.(29) In this current study, using the mixing tub lid clearly had the largest effect on baker's exposure as its use was less variable than divider oil, due to it being a relatively fixed engineering control measure. Possible explanations for this observation may be attributed to the fact that divider oil is not used during the entire shift or short-term tasks such as the production of "Portuguese" rolls or "Italian" breads that produce high flour dust exposures may dampen the

effect of divider oil. Furthermore, studies in the Netherlands have also shown a small reduction in flour dust levels with the elimination of dusting flour since substitution was often only partial. (31) In almost all cases substitutes were introduced whilst dusting flour was still used as part of the production process. However, in instances where sprinkling flour was totally eliminated, substantial reductions in exposure were observed. Studies in other sectors have also shown less than substantial reduction in exposures due to the substitution of dusty products with less dusty materials.(32)

In this study the demonstrated effectiveness of the mixing tub lid is consistent with large scale Dutch studies showing that control measures introduced during the weighing of ingredients, especially by limiting the use of bagged flour products and the enclosure of silo's (when dumping flour), strongly decreases exposure.(31) The important strength of this current study is that the lid was specifically designed so that it could be easily maintained and widely accessible for use in all other bakeries to promote future compliance with and long-term sustainability of the intervention beyond the study period.

As expected, workers who continued to shake bags during dough processing and employed high dusting instead of rubbing with flour showed an increase in exposures. This clearly demonstrated that work practices and worker behaviour during tasks have a great impact on exposure. This is a common finding of previous studies on exposure

control and interventions, which point to the importance of worker behaviour, skills and hygiene on exposure. (23,33)

Few studies have evaluated the specific impact of training in bakeries. A sector-wide intervention programme in Dutch bakeries aimed primarily at education of workers showed a rather limited effect on exposure levels.(18) The authors concluded that although workers' knowledge on the risk of flour dust exposure improved, this resulted in change in work practices only to a limited extent. In this current study, changes in work processes supplemented by technical aids emphasized during training, was associated with a substantial reduction in flour dust exposures. Furthermore, using either a crude measure of self-reported training or a more precise indicator of actual changes in work processes consistently showed a reduction. In this current study training of workers on its own was associated with a 54% reduction in flour dust levels. A recent review on the effectiveness of occupational health and safety training confirms that training promotes safer practices among workers and recommends that workplaces continue to deliver OHS training as part of a larger program. It cautions however that training alone will not necessarily prevent injuries and illnesses. (34) A strength of the current study is that the specific flour dust control training program that was developed has subsequently been incorporated into the overall bakery training programme. This will further enhance future compliance with and sustainability of the intervention over time.

The overall findings of this study demonstrated that the contribution of specific task-related control measures has a major impact on an individual level as well as the broader overall population exposures. Interventions in bakeries should therefore cover a range of tasks and control measures to have substantial impact on the population exposure distribution. The study also demonstrated that a multi-faceted approach of specific training accompanied by technical aids on correct flour handling practices substantially complemented other higher level control measures in reducing flour dust and allergen levels. This is similar to a message that has been emerging from other Institute for Work and Health systematic reviews, that multi-component programs are the key to effective prevention.(34)

One of the limitations of the study was the inability to resample the same workers who were previously assessed in the baseline exposure assessment survey, due to turn-over movement of workers between different jobs and turn-over of workers between bakeries. It was also not possible to completely separate the effect of individual control measures since they were highly correlated. Furthermore, the changes in work practices observed in the control group, and the consequent reduction in exposures in this group are indicative of a dilution effect and/or contamination among bakeries, as discussed. However, irrespective of these limitations, this study was able to show a significant intervention effect of the different strategies implemented. Due to the relatively short

(1 year) period of follow-up the study could not identify if the reduced levels were sustainable in the longer term.

CONCLUSION

This study has demonstrated that targeted interventions directed at individual workers within an identified high-risk population (eg, bread bakers) may prove to be more effective than large scale generic interventions. Further studies of this cohort are planned to determine the long term impact of the intervention strategies in sustained reduction of exposures and improved health outcomes in this group of bakers.

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The authors declare no competing interest.

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CHAPTER 8

DISCUSSION AND CONCLUSION

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CHAPTER 8

8.1 INTRODUCTION

Baker's asthma due to flour dust exposure in the work environment became increasingly prevalent in South Africa in the late 1990's due to the shift in location of bakeries, from large industrial bakeries and flour mills to in-store bakeries and supermarket stores.¹ The shift in growth of supermarket bakeries had also been reported in the United Kingdom, highlighting the problem in a group of workers not previously considered to be at increased risk of the disease.² This condition has become one of the most commonly reported manifestations of occupational asthma in both industrialized and rapidly industrializing countries and has shown no evidence of abatement.³

The increase in confirmed cases of baker's allergy and asthma and the consequent redeployment of 6% of bakers resulting in loss of productivity and increasing worker's compensation claims in this particular supermarket chain, which is the subject of this thesis, provided an opportunity to undertake a large scale investigation into the problem so as to identify interventions to reduce the health risks associated with flour dust exposures. Furthermore, a case report of fatal baker's asthma involving a bakery assistant, employed in a supermarket bakery of another chain store in the province, provided further impetus for these investigations.⁴

The papers included in this thesis provide a detailed insight into the relative prevalence of and risk factors for different asthma phenotypes, which informed the development of practical and focussed intervention strategies to reduce exposure to flour dust among these supermarket bakery workers.

A few papers have reported the need for an updated review of the literature (chapter 2) in order to develop a strong evidence for occupational

intervention and prevention programs.^{5,6,7} In order to develop effective control strategies for baker's asthma, it is essential to identify the extent of the disease burden and the environmental and host determinants of the disease (chapter 3-5), the relationship between exposure and health outcomes (chapter 6), and to measure the effectiveness of specific control measures (chapter 7) in reducing the incidence of asthma.

8.2 ASTHMA PHENOTYPES AND HOST DETERMINANTS

It is well-known that occupational exposure to flour dust is associated with the development of asthma. However, not all exposed workers develop occupational asthma. This suggests that the presence of underlying host susceptibility may be a potential risk factor in the context of high dust exposures. Atopy has been shown to be the most important host risk factor and modifier of allergic sensitisation and incident asthma-like symptoms among bakery apprentices.^{8,9,10} In this study of work-related asthma phenotypes in bakery workers, atopy was also significantly associated with probable occupational asthma. Aside from this being the most common phenotype (13%), Chapter 3 describes in more detail various other phenotypes of asthma that were characterised. These phenotypes were defined on the basis of asthma symptoms, airway hyper-responsiveness, atopic status and sensitisation to occupational allergens, not previously described in bakery workers. This association with atopy is highly suggestive of a dominant immune IgE-mediated mechanism underlying this particular phenotype. The subsequent study (Chapter 4) confirmed the role of sensitisation to cereal flour allergens as being the major determinant of elevated fractional exhaled nitric oxide (FeNO) levels, a marker of allergic airway disease, with atopy and current smoking status modifying this relationship in opposite directions.

In the current study, only approximately half of the proportion of work-related symptoms could be attributable to wheat sensitisation. Whilst wheat is considered to be one of the most important occupational allergens, there are other allergens in the baking environment that have been implicated in allergic reactions (chapter 2). Interestingly in this current study, a relatively large proportion (33%) of workers reported work-related asthma symptoms specifically to rye flour, despite this flour constituting a small proportion (<10%) of products handled in these bakeries and enzymes not appearing as prominent as has been reported in industrialised countries.¹¹ This can be attributed mainly to cross-reactivity between grain cereal allergens,¹² or an additional irritative effect of rye flour, as demonstrated by its ability to produce a greater bronchial response compared to wheat.¹¹ Aside from additive enzymes such as alpha amylase that played a minor role in the causation of symptoms in this group of bakers, several other salt-soluble proteins, salt-insoluble storage proteins and recombinant proteins have also been identified as allergens associated with baker's asthma.^{8,13} The role of these allergens were however not tested in our study. Further research into the relevance of other potential allergens in this population is needed in order to understand whether there are other pathophysiological mechanisms that may be involved in causing symptoms reported.

8.3 EXPOSURE CHARACTERISATION AND DETERMINANTS

Detailed information on individual particulate dust exposures and their relationship to the major allergens (wheat, rye, alpha amylase) of interest were presented in Chapter 5 of this thesis. In the light of current evidence as reported in the literature, the use of integrated exposure data to assess effectiveness of pre-existing exposure control measures and the development of predictive exposure models for use in epidemiological analysis is rare. While exposure to wheat and fungal alpha-amylase allergens among bakery workers has been well described, exposures to rye flour allergens and its role in baker's asthma is also less well documented.

This was the first study to document occupational exposure to rye allergens among supermarket bakery workers. An increasing number of studies, mainly case reports, have in more recent years reported rye flour allergens as an important cause of baker's asthma.^{11,14,15} Among these is a report of baker's asthma in a worker employed in a supermarket chain store of this study population. This current study provided further evidence for a potentially emerging role of rye flour allergens in baker's asthma, and merits further investigation in this and other populations with increasing use of rye flour to meet the increasing demand for rye bread products globally.

The detailed exposure characterisation further demonstrated that bread bakers had the highest average exposures for flour dust particulate, wheat, and rye allergens, whilst levels of alpha-amylase allergens were below the limit of detection for several occupational titles. This confirmed the findings of a low prevalence of sensitisation to alpha amylase (4%) in this population, and that these enzymes were not used in large quantities compared to other settings. Further exploration of environmental factors also allowed for identification of exposure determinants to prioritise potential areas for intervention. Specific job types and certain tasks were identified as the most important source of variability in dust and allergen concentrations and were therefore the main focus of the interventions that were subsequently designed. The exposure data also provided the baseline exposure estimates for the intervention study that is described in greater detail in Chapter 7. Furthermore, the predictive models that were developed using this data provided a relevant exposure metrics for personal exposures to wheat allergens used in exploring exposure-response relationships as described in Chapter 6.

8.4 EXPOSURE-RESPONSE RELATIONSHIPS

This study demonstrated that the level of exposure to allergens is an important determinant of allergic sensitisation and probable occupational

asthma based on objective measures of lung function such as airway hyper-responsiveness that was used in this current study. The exposure-response relationships for average exposure followed a bell-shaped curve, with the prevalence of sensitisation, allergic symptoms and probable occupational asthma, increasing up to 10 - 15 $\mu\text{g}/\text{m}^3$ of wheat allergen concentration, reaching a plateau and then decreasing at higher concentrations. This finding is in agreement with previous studies of populations in Sweden and the Netherlands.^{16,17} The strong associations between exposure and allergic health outcomes further suggested that the incidence of sensitisation could effectively be reduced through interventions aimed at decreasing allergen exposure levels.

Further attempts were made to explain the bell-shape exposure-response curve by exploring a possible protective role of IgG4 in mediating this relationship as has been suggested by some studies of laboratory animals.¹⁸ However, no protective effect was demonstrated and it was concluded that the healthy worker effect was a more plausible explanation for the pattern observed. Recent studies have alluded to the role of protective cytokines such as IL-10,^{19,20,21,22} that could attenuate the exposure-response relationship. It was not possible to determine the potential role of these cytokines since these markers were not measured in the current study. It is recommended that further studies investigate the non-linear dose-response relationships observed in most studies to date in the light of new knowledge in recent years on the effects of immunotherapy and the development of immune tolerance observed in subjects undergoing this treatment.

This thesis has also contributed to the growing knowledge base that could be used for standard setting agencies tasked with developing occupational exposure limits. The exposure characterisation studies reported in this thesis have shown a strong correlation ($r=0.84$) between inhalable flour dust and wheat allergens, suggesting that flour dust levels could be used as a proxy for allergen exposures (chapter 5). Furthermore, a high prevalence of wheat

sensitisation (26%) (Chapter 3) was demonstrated in this population, even though workers were exposed to mean flour dust levels of 0.8mg/m^3 ($6.7\mu\text{g/m}^3$ wheat allergen). This is consistent with other studies of supermarket bakery workers reported in the UK.²³ The exposure response modelling in this current study also showed that the prevalence of sensitisation and other clinically relevant endpoints increased up to a level of $10\mu\text{g/m}^3$ suggesting that occupational exposure limits currently being used in South Africa for grain particulate dust (10mg/m^3) is inappropriate and therefore not protective for bakery workers. The Health Council of the Netherlands has emphasised that an occupational exposure limit (OEL) should prevent against allergic sensitization, since sensitization plays a crucial biological role and is a prerequisite for the development of allergy leading to asthma.²⁴ With the advances in exposure assessment and results from exposure-response models several countries have re-evaluated their exposure standards for flour dust. This has led the American College of Governmental Industrial Hygienists (ACGIH) to adopt a threshold limit value for inhalable flour dust of 0.5mg/m^3 .²⁵ A report of the Health Council of the Netherlands suggests that no evidence of a threshold level has been observed for (wheat) flour dust, even at low levels of exposure.^{26,27} As a result, an alternative approach that calculates the excess risk at a range of exposure levels has been suggested. According to this approach an excess sensitization risk from 1% to 10% occurs at exposure levels of 0.12 and 1.2mg/m^3 respectively, suggesting that the agreement on what excess risk is acceptable will be influenced by social partners over time.²⁸

8.5 INTERVENTIONS IN SUPERMARKET BAKERIES

Chapter 7 provides an exposé of different intervention strategies that were introduced in these supermarket bakeries for improved flour dust control to achieve primary prevention of occupational asthma based on the knowledge gained from the health outcome, exposure characterisation and dose-response studies.²⁹ There are few well-designed intervention studies, with

the exception of the Minnesota wood dust study,³⁰ that report detailed exposure characterisation to determine the effect of exposure reductions for occupational asthma.^{29,31} As has been reported, there are no studies that describe the effectiveness of focussed interventions specifically in bakeries, although information from previous studies in Dutch bakeries have provided an indication of possible control measures to implement.

This is the first intervention study to demonstrate a substantial overall reduction in inhalable flour dust particulate (50%), wheat (56%) and rye (61%) allergen exposure in bakeries. The study also demonstrated that a multi-faceted approach of specific training accompanied by technical aids on correct flour handling practices, an 80% reduction in flour dust and allergen exposures is achievable. The overall reduction in dust exposures found in bakeries were much greater than those observed in the Minnesota wood dust study (26%)³⁰ and a pragmatic intervention study in the Dutch bakery industry (2%).³² The findings of the current study suggests that tailored interventions directed at individual workers within an identified high-risk population such as bread bakers may prove to be more effective than large scale generic interventions for bakeries. Its novel contribution is its specific focus on the evaluation of different control strategies on dust exposures in bakeries. Furthermore, significant reductions were not only observed among bakers, but across all jobs since the entire environment was less dusty following control of high dust exposure tasks. This demonstrated that the contribution of specific task-related control measures had a significant impact at an individual level as well as on the broader overall bakery store population exposures. It could therefore be expected that the exposure reductions would have an impact on reducing the disease burden in this population as well. Further studies of this cohort are needed to determine the extent to which these strategies result in a sustained reduction of exposures and disease burden in these bakeries.

It is well recognised that quantitative evaluations of the health impact of intervention strategies may in themselves prove to be limiting and inefficient due to study design issues. As a result, dynamic population models have been used to predict the effect of intervention strategies on disease burden. These models have suggested that the impact of most interventions was rather limited, achieving an overall effect of less than 50% for lower respiratory symptoms and asthma after 20 years.³³ Other models suggest that a rigorous health surveillance strategy that identifies workers who are sensitised or report upper respiratory symptoms and are subsequently removed from exposure, would result in a 60% decreased disease burden after 20 years. Model simulations based on 2% exposure reduction reported in an earlier intervention program, showed an overall effect of only 25% over 20 years. This reduction in exposure of 2% is however much lower than the 50% reduction achieved in this current study over a period of 12 months, suggesting a much improved model performance were the data in this current study to be used. It is probable that the impact on disease burden in this current study prioritising workplace control measures could be more substantial than an approach based on rigorous health surveillance in the previous models. This is based on the assumption that the reduction in exposure levels will be sustained over time, since the mixer lid and training program has been integrated into all bakeries according to company policy.

More recent studies have sought to develop more efficient approaches to medical surveillance by applying diagnostic models to predict the probability of sensitisation and work-related symptoms in workers exposed to flour dust allergens.^{34,35} Suarathana et al³⁵ showed that a simple model reliant on questionnaire items can be used to stratify bakers based on the probability of them being sensitised to wheat allergens. Whilst the study by Meijer et al³⁴ demonstrated that a simple questionnaire model used to predict the probability of wheat sensitisation, resulted in the accurate detection of 90% of workers with baker's asthma. The application of these models, allows for the identification of high-risk individuals that could be subjected to further

clinical evaluation, thereby increasing the cost-effectiveness of medical surveillance programs aimed at secondary prevention.

However, these apparently successful approaches using rigorous medical surveillance to identify “high-risk” individuals, on their own have limitations in that they introduce a false sense of security to “low” risk workers; they are in conflict with the ALARA principle (As Low As Reasonably Attainable) and more importantly exposure reduction aimed at individual level may not be as effective and efficient as the findings of this current study suggests. Furthermore, previous studies in supermarket bakeries have shown that symptom-based questionnaires are relatively insensitive in the routine surveillance of bakery employees.^{36,37} Therefore, while these models may have a higher diagnostic accuracy their value in the periodic examination of bakers at risk other than cost effectiveness may be limited.

This thesis has demonstrated sufficient evidence to suggest that intervention programs should primarily focus on targeted exposure reduction strategies as they have been shown to have a significant impact on flour dust levels. Furthermore, the reduction in exposures combined with predictive models to identify high-risk workers may be a more rational approach in decreasing the risk and disease burden in bakery workers.

8.6 LIMITATIONS

One of the major issues to consider with cross-sectional epidemiological studies on respiratory health outcomes such as the current study is the *selection bias* caused by the healthy worker effect. There are many factors that influence the healthy worker effect in occupational populations. The first relates to pre-employment selection in which individuals with respiratory symptoms tend to not choose jobs that may further worsen their respiratory condition should they already be asthmatic for example, or are selected out

through pre-employment screening by occupational health services. A review of company policies suggested that this factor was unlikely to play a major role in this study. However, a second possible selection effect that occurs commonly during employment, whereby bakers with allergic symptoms are redeployed to lower exposed jobs, or completely leave employment due to their asthma, did play a role in our study. In this current study 6% of bakers reported being redeployed from their jobs due to their asthma symptoms (Chapter 3). In an attempt to minimize the potential bias introduced by these selection effects, ex-bakers with asthma who had been relocated from the bakery section two years prior to the study were also included in the study. As indicated earlier in the discussion, it is likely that the exposure-response relationships demonstrated in our study (Chapter 6) may nevertheless have been influenced by selection effects since the exposure estimates used in these models were based on current exposures and not on exposure concentrations when asthma symptoms first developed. Previous studies that measured cumulative exposure have shown that the development of symptoms may be influenced by level and duration of exposure.¹⁷ The magnitude of this selection bias can only be investigated in longitudinal studies of bakery workers, which is a subject for future research since this has not been studied in great detail.

It is possible that information recall bias may have been introduced during the questionnaire assessment of respiratory health outcomes, due to possible under-reporting by those workers with symptoms, for fear of losing their jobs or being redeployed. It is unlikely that this played a major role in this study as the prevalence of occupational asthma (13%) is very similar to other studies reported in literature.^{38,39} Furthermore, the exposure-response relationships were based on objective health outcomes such as allergic sensitization and non-specific bronchial hyper-responsiveness, which followed similar patterns to outcomes that used only symptoms in their case definition (Chapter 6).

With specific reference to sensitization and respiratory health outcomes, variables such as atopy, age, gender and smoking status have been associated with sensitisation or occupational asthma in various studies.⁴⁰ These covariates were evaluated in great detail and where appropriate were treated as confounding variables and controlled for in all the statistical analysis procedures. However, it cannot be totally excluded that some bias may have occurred due to error in the measurement of these confounders.

Despite the overall findings of this thesis demonstrating a beneficial effect of the focussed interventions specifically designed for these bakeries, it is likely that the estimate of the intervention effect may have been attenuated by a decrease in exposure gradient between the intervention and control group due to greater than 50% reduction in exposures found in both groups. This suggests that there was probable contamination of the control group and based on the findings of our workplace inspection audits to assess adherence to the intervention, the unplanned introduction of co-interventions in both the intervention and control groups. It is likely that this was as a result of increased awareness among all workers of the health risks of flour dust, by virtue of participation in the study, resulting in them adopting safer work practices to lower dust exposures. The relocation of affected workers as well as the transfer of managers from intervention sites to control sites further contributed to diluting the intervention effect as it resulted in increased homogeneity between groups. However, while this was not desirable for the experimental design approach that was used, from a public health perspective the adoption of safer work practices across all groups and the resultant reduction of exposures, may in the long term lead to a reduction in sensitization and occupational asthma in this population, contributing to a positive overall impact of this research.

8.7 THE IMPACT OF THIS RESEARCH

Asthma is an important public health problem with high morbidity and economic burden in the occupational context. Workers with occupational asthma have a poor prognosis if not identified early and removed from exposure. This leads to loss of productivity and loss of skills in an ever increasingly competitive labour market. This research study identified risk factors for allergic sensitisation to occupational flour allergens and demonstrated viable intervention strategies to reduce the risk in bakeries. These encompassed novel engineering controls; improved work practices through training; and the use of appropriate personal protective equipment for certain high risk tasks. In this way, the study identified the most effective preventative strategy to decrease the risk of allergic respiratory disease in supermarket bakery workers.

The experience gained in this study has also enabled the development of more appropriate industrial hygiene monitoring techniques and medical surveillance protocols for supermarket bakery workers to be used by occupational health service personnel. The health and safety training instruments, including the video and handbook on flour dust control that was developed for the study, have subsequently been integrated into the general induction and on-going training programme for all workers to ensure ongoing awareness on the need for dust control. Finally, the prototype mixer tub lid specifically designed for the intervention group of bakeries has subsequently been introduced into all bakeries of this supermarket chain nationally as a result of the favourable results obtained through this large scale intervention study.

It is envisaged that the findings of this study will provide the impetus for changing the legislation in relation to exposure standards for flour dust under the Hazardous Chemical Substances Regulations of the Occupational Health and Safety Act (OHSA) in South Africa (1993), which is currently being

revised. Recommendations will be made to the Department of Labour to introduce a more appropriate and protective exposure standard specifically for flour dust so as to contribute towards reducing the burden of occupational allergy and asthma among bakery workers in South Africa.

8.8 CONCLUSION

This thesis has demonstrated that occupational allergy and asthma due to inhalation of flour dust allergens is a significant problem in supermarket bakeries. It has confirmed that sensitisation to wheat flour allergens is the most important predictor of airway inflammation. This study has also provided detailed insights into the host risk factors associated with various clinical phenotypes of asthma in bakery workers, the knowledge of which is important in guiding on-going medical surveillance and clinical management of bakery workers. Detailed characterisation and quantification of flour dust and allergen exposures enabled further investigation of exposure-response relationships for wheat allergen exposures and the potential role of IgG4 in this relationship. These models confirmed the increased risk of sensitization and allergic respiratory disease associated with increasing exposure to wheat allergens, implying that the incidence of both these clinical endpoints can be reduced by improving flour dust control. The study demonstrated that a focused multi-pronged intervention strategy can have a significant impact on the reduction of flour dust and allergen exposures in bakeries. In the light of the scientific evidence provided it is likely that should these reductions in exposures be sustained over the long term, the potential to reduce the disease burden in this population could be substantial.

8.9 REFERENCES

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APPENDICES

University of Cape Town

APPENDIX 1

University of Cape Town

**PRODUCT INFORMATION FOR SUPERMARKET BAKERIES IN THE
WESTERN CAPE OF SOUTH AFRICA**

SUPPLIER: BAKELS		
PRODUCT	FUNCTIONALITY	INGREDIENTS
Bun Mix	Bun mix is a composite improver of superior quality and it ideal for production of American hamburger buns, hot dog buns and confectionery lines	Sucrose Vegetable fat Sodium chloride - Soya flour - Emulsifiers - Gluten - Bread improvers - Anti-caking agents - Enzymes
Extra soft premix	-is a composite premix for the manufacture of soft rolls, morning goods and fancy breads	Sucrose Vegetable fat Sodium chloride - Soya flour - Emulsifiers - Bread improvers - Wheaten flour - Enzymes
Bread mix	- is an all-in-one premix developed for the production of white bread an brown standard bread	Sucrose Vegetable fat Sodium chloride - Soya flour - Emulsifiers - Bread improvers - Wheaten flour - Enzymes Anti-caking agents
Apito sunseed bread mix	- is a complete mix requiring only the addition of yeast and water to produce a superior health loaf containing whole wheat and selected seeds	Sucrose Vegetable fat Sodium chloride - Wheat flour - Emulsifiers - sunflower seed - linseed - Crushed Wheat - Gluten - colourant Calcium acetate Milk solids Antioxidant

SUPPLIER: BAKELS		
PRODUCT	FUNCTIONALITY	INGREDIENTS
Light rye mix	- is a complete premix requiring only addition of yeast and water to produce a light rye bread	Sucrose Rye flour Malt flour Sodium chloride - Wheat flour - Caraway seeds - acidifying agent - enzymes Gluten - Bread improvers Anti-caking agents
Bagel mix	- is a premix to produce a traditional Bagel thought to originate from Eastern Europe	Sucrose Malt flour Sodium chloride - Wheat flour - Soya flour - enzymes Gluten - Bread improvers Anti-caking agents Vegetable fat
Stoneground premix	- is a premix requiring only the addition of flour, yeast and water to produce bread and rolls	Rye flour Sodium Chloride Sucrose Vegetable fat Wheat flour Milk solids - Emulsifiers - Soya flour

SUPPLIER: AUSTRALIAN PREMIX BAKING CO.		
Kornspitz mix		wheat flour backaldrin rye mix consisting of various flours groats and flakes bran seeds bread spices backaldrin rye bread improver enzymes emulsifiers
Australian rye mix		rye flour white bread flour crushed rye backaldrin bread spice backaldrin dry sour backaldrin bread improver enzymes emulsifiers
Rye mix		rye flour backaldrin bread spice backaldrin dry sour backaldrin bread improver enzymes emulsifiers salt
Vienna rye roll mix		rye flour cake flour backaldrin bread spice backaldrin dry sour backaldrin bread improver enzymes emulsifiers salt

SUPPLIER: AUSTRALIAN PREMIX BAKING CO		
PRODUCT	FUNCTIONALITY	INGREDIENTS
Malt rye mix		rye flour white bread flour backaldrin bread spice backaldrin dry sour backaldrin bread improver enzymes emulsifiers salt caraway seeds
Finnbread mix		rye flour whole wheat flour crushed rye backaldrin bread spice backaldrin dry sour backaldrin bread improver enzymes emulsifiers salt sugar sunflower seeds linseeds

TIGER MILLING & FATTIS MONIS

Cake flour, White bread, Brown bread, Nutty Wheat, Crushed Wheat

APPENDIX 2

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENGLISH CONSENT FORM

1. **Title of research project**

Occupational risk factors and interventions for reducing the incidence of allergy and asthma among bakery workers in the Western Cape.

2. **Purpose of the research**

The University of Cape Town is conducting this important study of the allergic effects of exposure to flour dust. This study is going to be done by researchers who are independent of the company. We will be studying a group of workers who have been involved with baking process. It is hoped that this study will provide greater insight into the risk factors for allergic sensitization among bakery workers and identify appropriate preventative strategies to be implemented in order to reduce the incidence of allergy and asthma among bakery workers.

3. **Description of the research project**

If you agree to participate you will be asked to complete the following tests during working time:

- a) **Complete a questionnaire.** A member of our study team will interview you in privacy to complete the questionnaire. You will be asked questions about any breathing or chest problems; current and previous employment history, working with flour and dietary history.
- b) **Skin tests**
Skin tests will be done to see whether you are allergic to any of the flour extracts or any other substance that commonly causes allergy in the Western Cape. A nurse will place a drop of liquid containing each type of flour allergen and the other substances on your forearm and then use a lancet to scratch the skin in that area.
- c) **Blood test**
You will also be asked to undergo a blood test to check for allergies to specific flour allergens. Ten ml (about two teaspoons) of blood will be drawn once by a nurse.
- d) **Breathing tests**
You will be asked to blow several times into a machine which measures how well your lungs are working. You will be asked to repeat the breathing test after you first breathe in a small amount of a chemical substance (methacholine). This test helps us find out if you may have a breathing problem like asthma. You may be asked to breathe in this substance and then blow into the machine several times.

4. **Confidentiality of information collected**

Your name will not appear in any reports on this study. The records of skin tests, blood tests, questionnaires and breathing tests will be kept completely confidential and will be seen only by members of the study team.

5. **Risks and discomforts of the research**

- a) **From the blood tests.** You will feel a single needle stick when the blood is taken. Sometimes a small bruise may occur from the needle stick, but this is minor and will heal quickly. The total amount of blood taken is quite small and your body will quickly replace it.
- b) **From the questionnaire and breathing tests.** From the questionnaire and breathing tests. There are no risks from completing the questionnaire. There is a small chance that the initial breathing test could cause you to become light-headed or faint. Having you complete the test in a seated position under the observation of trained personnel greatly reduces the chance of your having such a problem. Part of the breathing test uses a chemical substance that can cause headache, cough, chest tightness, hoarse voice or a sore throat for a short time in some people. Very rarely it can cause severe breathing problems. Such breathing problems almost always can be treated successfully immediately with a different medication, which you breathe in. You will only be given the chemical substance if your simple breathing test is normal. This greatly reduces the chance of having a serious problem. These tests will be carried at the Lung Institute with medical personnel knowledgeable in the treatment of such problems immediately available.
- c) **From the skin tests.** Itchiness can occur in some instances. Very rarely severe allergic reactions to skin tests (difficulty breathing or feeling faint and collapsing) may occur in people that are highly allergic. You will be asked questions before receiving the tests to help make sure you are not at any risk for such a problem. In addition, you will be at the Lung Institute, where nurses will be available to check you for any possible problems, for several hours after the test and have medications on hand to treat any such reaction. A doctor is also located nearby and ready to help if necessary.

6. **Expected benefits to you and to others**

You will be given a written copy of all your test results along with an explanation of what they mean, unless you tell us that you do not wish to receive this. You may wish to show these to your doctor if you are having any problems. These tests will help determine if you have an allergy to flour or other substances used in the skin tests. What we learn from this study will help to protect you, and those working with flour in South Africa and other parts of the world. We will learn how best to monitor worker's health and how to reduce workers' exposure to flour allergens.

7. **Costs to you resulting from participation in the study**

The study is offered at no cost to you. In the event a problem is discovered and you wish to be seen by a doctor for it, we can recommend to you who to see. However, the study cannot pay for these additional medical visits or treatments.

8. **Contact person.**

You may contact one of the following persons for answers to further questions about the research, your rights, or any injury you may feel is related to the study.

University of Cape Town Researchers:

Dr. Mohamed Jeebhay, Telephone No. (021) 406-6309

Roslyn Baatjies, Telephone No.: (021) 406-6665

University of Cape Town Research Ethics Committee:

Ms. Xolile Fula (Ethics Administrator) (021) 406-6492

University of Cape Town

**UCT OCCUPATIONAL ALLERGY AND ASTHMA AMONG
BAKERY WORKERS STUDY IN WESTERN CAPE OF SOUTH
AFRICA**

ENGLISH CONSENT FORM

STUDY NO. _____

9. Consent of the participant

I have read the information given above, or it has been read to me. I understand the meaning of this information, Dr./Mr./Ms.

_____ has offered to answer any questions concerning the study. By signing this form, I hereby consent to participate in the study. I also understand that I am free to withdraw from the study at any time without penalty.

10. Documentation of the consent

One copy of this signed document will be kept together with our research records for this study. A copy of the information sheet about the study will be given to you to keep.

Printed name of participant

Signature, Mark, or Thumb Print

Interviewer's name (Print)

Signature

DATE: _____

APPENDIX 3

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENGLISH QUESTIONNAIRE

Card 1

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 1-3

Survey Number _____

A. IDENTIFICATION DATA

1. Surname _____

2. First name/s _____

3. Address _____

4. Work number _____

5. Date of birth: Day _____ Month _____ Year _____

6. Gender: Male (1)
 Female (2)

7. Home Language: English (1)
 Afrikaans (2)
 Xhosa (3)
 Other (4)

8. Interviewer's initials _____

9. Date of interview: Day _____ Month _____ Year _____

10. Bakery: _____

11. Are you a casual or permanent worker?
 Casual (1)
 Permanent (2)

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 4-9

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 10-15

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 16

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 17

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 18

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 19-24

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 25-26

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 27

B.HEALTH PROBLEMS

Wheeze and tightness in the chest

1. Have you ever had wheezing or whistling in your chest in the past?

Yes (1)

No (2)

☐ 28

If YES, go on to Question 1.1

If NO, skip to Question 2

1.1 If yes, when was the first time you had these symptoms.

Date: Month _____ Year _____

☐☐☐☐ 29-32

1.2 Have you had wheezing or whistling in your chest at any time in the **last 12 months?**

Yes (1)

No (2)

☐ 33

If YES, go on to Question 1.2.1

If NO, skip to Question 2

1.2.1 Have you been short of breath when the wheezing noise was present?

Yes (1)

No (2)

☐ 34

1.2.2 Have you had this wheezing or whistling when you did not have a cold or flu?

Yes (1)

No (2)

☐ 35

2. Have you been woken up with a feeling of tightness in your chest at any time in the **last 12 months?**

Yes (1)

No (2)

☐ 36

Shortness of breath

3. Have you had an attack of shortness of breath that came on during the daytime when you were at rest at any time in the **last 12 months?**

Yes (1)
No (2)

☐ 37

4. Have you had an attack of shortness of breath that came on following running or exercise at any time in the **last 12 months?**

Yes (1)
No (2)

☐ 38

5. Have you been woken by an attack of shortness of breath at any time in the **last 12 months?**

Yes (1)
No (2)

☐ 39

Cough and phlegm from the chest

6. Have you been woken by an attack of coughing at any time in the **last 12 months?**

Yes (1)
No (2)

☐ 40

7. Do you usually cough first thing in the morning?

Yes (1)
No (2)

☐ 41

8. Do you usually cough during the rest of the day, or at night?

Yes (1)
No (2)

☐ 42

If YES, go on to Question 8.1

If NO, skip to Question 9

8.1 Do you cough like this on most days/nights for as much as three or more months in each of the last two years?

Yes (1)
No (2)

☐ 43

9. Do you usually bring up any phlegm from your chest first thing in the morning?

Yes (1)

No (2)

☐ 44

10. Do you usually bring up any phlegm from your chest during the day, or at night?

Yes (1)

No (2)

☐ 45

If YES, go on to Question 10.1

If NO, skip to Question 11

10.1 Do you bring up phlegm like this on most days/ nights for as much as three or more months in each of the last two years?

Yes (1)

No (2)

☐ 46

Breathing

11. Do you ever have trouble with your breathing?

Yes (1)

No (2)

☐ 47

If YES, go on to Question 11.1

If NO, skip to Question 12

11.1 Do you have this trouble:

☐ 48

Give all options at once

Insert a cross (X) next to one answer only

a) continuously so that your breathing is never quite right? _____

b) repeatedly, but it goes away completely between the times when it troubles you? _____

c) only rarely? _____

12. Are you disabled from walking by a condition other than heart or lung disease?

☐ 49

Yes (1)

No (2)

If YES, state the condition _____
and go on to Question 13
If NO, go to Question 12.1

12.1 Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill?

Yes (1)

No (2)

☐ 50

If YES, go on to Question 12.1.1

If NO, skip to Question 13

12.1.1 Do you get short of breath walking with other people of your own age on level ground?

Yes (1)

No (2)

☐ 51

12.1.1.1 Do you have to stop for breath when walking at your own pace on level ground?

Yes (1)

No (2)

☐ 52

Asthma

13. Have you ever had asthma?

Yes (1)

No (2)

☐ 53

If YES, go on to Question 13.1

If NO, skip to Question 13.8

13.1 If yes, was this confirmed by a doctor?

Yes (1)

No (2)

☐ 54

13.2 How old were you when you were told you have asthma?

☐ 55

Give all options at once

Insert a cross (X) next to one answer only

- a) Only before you were 17 years old _____
- b) Only at the age of 17 years or older _____
- c) Both _____

The following references to "attack" of asthma refers to episodes of wheezing, shortness of breath, chest tightness or cough attributed to asthma

13.3.1 How old were you when you had your first attack of asthma?

_____ years old

56-57

13.3.2 How old were you when you had your most recent attack of asthma?

_____ years old

58-59

13.4.1-6 Which months of the year do you usually have attacks of asthma?

13.4.1 January/February

Yes (1)

No (2)

☐ 60

13.4.2 March/April

Yes (1)

No (2)

☐ 61

13.4.3 May/June

Yes (1)

No (2)

☐ 62

13.4.4 July/August

Yes (1)

No (2)

☐ 63

13.4.5 September/October

Yes (1)

No (2)

☐ 64

13.4.6 November/December

Yes (1)

No (2)

☐ 65

13.5 Have you had an attack of asthma in the last **12 months?**

Yes (1)

No (2)

☐ 66

If YES, go on to Question 13.5.1

If NO, skip to Question 13.6

13.5.1 How often have you had an attack of asthma in the **last 12 months?**

☐ 67

Give all options at once

Insert a cross (X) next to one answer only

a) Every day

b) More than 2 times a week

c) More than 1 time per month

d) 3 to 12 times in the whole year

e) 1 to 2 times in the whole year

13.6 Are your chest symptoms caused by, or made worse by any of the following:

Answer all questions

13.6.1 Contact with animals/pets

Yes (1)

No (2)

☐ 68

13.6.2 Grass or flowers

Yes (1)

No (2)

☐ 69

13.6.3 Heavy exercise

Yes (1)

No (2)

☐ 70

13.6.4 Breathing cold air

Yes (1)

No (2)

☐ 71

13.6.5 Dusts or sprays at work

Yes (1)

No (2)

☐ 72

13.6.6 Tobacco smoke

Yes (1)
No (2)

☐ 73

13.6.7 Change in the weather

Yes (1)
No (2)

☐ 74

13.7 Do your chest symptoms seem better or worse when you are away from work (for example, on weekends, off-shift and vacations)?

☐ 75

Give all options at once
Insert a cross (X) next to one answer only

- a) Stay the same _____
b) Get better _____
c) Get worse _____

13.8 Does being at work ever make your chest tight or wheezy?

Yes (1)
No (2)

☐ 76

If YES, go on to Question 13.8.1
If NO, skip to Question 13.9

13.8.1 When did you first notice having problems with chest tightness or wheeze at work?

Date: Month _____ Year _____

☐☐☐☐ 77-80

13.8.2 Is there anything that you work with that causes you to have these chest symptoms?

Yes (1)
No (2)

Card 2
☐ 1

If YES, go on to Question 13.8.3 (**specify wheat, rye &/or premix**) or any other substance
If NO, skip to Question 13.9

13.8.3 What do you think is causing these symptoms?

☐ 2

13.9 Have you ever had to change or leave your work area, either temporarily or permanently, in this bakery or any other bakery because of any chest symptoms?

Yes (1)

No (2)

☐ 3

If YES, go on to Question 13.9.1

If NO, skip to Question 13.10

13.9.1 What type of job were you doing when this happened?

☐ 4-5

13.9.2 Was this a job in this bakery?

Yes (1)

No (2)

☐ 6

If YES, go on to Question 13.9.2.1

If NO, skip to Question 13.10

13.9.2.1 What area/section did you move to?

☐ 7-8

13.9.2.2 What job did you do there?

☐ 9-10

13.9.2.3 Did your symptoms improve when you changed jobs?

Yes (1)

No (2)

☐ 11

13.10 Have you ever worked in a job or jobs that exposed you to vapours, gas, dust or fumes?

Yes (1)

No (2)

☐ 12

If YES, go on to Question 13.10.1.

List the jobs beginning with the most recent

If NO, skip to Question 13.11

13.10.1 What was or is this job? _____
(if current job write 'current job')

☐ 13-14

13.10.2 Before that? _____

☐ 15-16

13.10.3 Before that? _____

☐ ☐ 17-18

13.11 Has there ever been an instance when you inhaled a large amount of vapour, gas, dust or fumes in any of these jobs that resulted in you developing a tight chest, wheeze or cough?

Yes (1)

No (2)

☐ 19

If YES, go on to Question 13.11.1.

If NO, skip to Question 13.12

13.11.1 What was or is this job? _____
(if current job write 'current job')

☐ ☐ 20-21

13.12 Are you using any medicines, including inhalers/ pumps, nebulizers, syrups or tablets, for asthma or breathing problems?

Yes (1)

No (2)

☐ 22

If YES, go on to Question 13.12.1, showing examples of each

If NO, skip to question 13.13

13.12.1 Which medicines?

☐ 23
☐ 24
☐ 25

13.12.2 Do you take these medicines every day even when you do not have any trouble breathing?

Yes (1)

No (2)

☐ 26

13.13 Have you ever been treated for any of the following:

Answer all questions

13.13.1 Repeated chest infections as a child

Yes (1)

No (2)

UNK (3)

☐ 27

13.13.2 Tuberculosis (TB)

- Yes (1)
No (2)
UNK (3)

☐ 28

13.13.3 Chronic bronchitis

- Yes (1)
No (2)
UNK (3)

☐ 29

Nose and eye symptoms

14. Have you ever had any nose or eye problems or allergies such as hay fever?

- Yes (1)
No (2)

☐ 30

If YES, go on to Question 14.1 Answer all questions
If NO, skip to Question 14.4

14.1 How old were you when you first noticed these symptoms?

_____ years old

☐ ☐ 31-32

14.2 During the past 12 months have you had two or more episodes of:

14.2.1 sneezy, itchy or runny nose when you did not have a cold or flu?

- Yes (1)
No (2)

☐ 33

14.2.2 red, itchy or watery eyes

- Yes (1)
No (2)

☐ 34

14.2.3 Do you usually have the nose or eye symptoms at any particular time of the year?

- Yes (1)
No (2)

☐ 35

14.2.3.1 If YES, which is the worst season?

☐ 36

Give all options at once
Insert a cross (X) next to one answer only

- a) Winter _____
- b) Spring _____
- c) Summer _____
- d) Autumn _____

If YES to any of the above in question 14.2, go on to Question 14.3
If NO, skip to Question 14.4

14.3 Do your nose or eye symptoms seem better or worse when you are away from work (for example, on weekends, off-shift and vacations)?

☐ 37

Give all options at once
Insert a cross (X) next to one answer only

- a) Stay the same _____
- b) Get better _____
- c) Get worse _____

14.4 Does being at work ever cause you to have sneezy/itchy/runny nose or red/itchy/watery eyes?

- Yes (1)
- No (2)

☐ 38

If YES to any one of the above, go on to Question 14.4.1
If NO, skip to Question 14.5

14.4.1 Since when have you been having these symptoms at work?

Date: Month ____ Year ____

☐☐☐☐ 39-42

14.4.2 Is there anything that you work with that causes you to have these symptoms?

- Yes (1)
- No (2)

☐ 43

If YES, go on to Question 14.4.3 (**specify wheat, rye &/or premix**)
or any other substance
If NO, skip to Question 14.5

14.4.3 What do you think is causing these symptoms?

☐ 44

14.5 Are you using any medicines, including nose sprays, drops, tablets or injections, for any nose or eye symptoms at present?

Yes (1)

No (2)

☐ 45

If YES, go on to Question 14.5.1

If NO, go on to Question 14.6

Present a chart with different samples of allergy medicines (N.B. a worker might show you his/her medicines).

14.5.1 Which medicines?

☐ 46

☐ 47

14.6 Did you have hay fever (itchy or watery eyes/nose) as a child?

Yes (1)

No (2)

☐ 48

Skin symptoms

15. Have you ever had any kind of skin problem either at home or at work?

Yes (1)

No (2)

☐ 49

If YES, go on to Question 15.1

If NO, skip to Question 15.4

15.1 How old were you when you **first** noticed this skin problem?

_____ years old

☐ ☐ 50-51

15.2 During the past **12 months** have you had any skin problems that occurred **2 or more times**?

Yes (1)

No (2)

☐ 52

If Yes, which of the following problems did you have?

Go through each option in the table below and circle the appropriate response.

	Forearms	Whole
	Hands	Body
15.2.1		
itchy or	Yes/No	Yes/No
scratchy skin		
15.2.2		
hives	Yes/No	Yes/No
("bommels")		
15.2.3		
dry, scaly	Yes/No	Yes/No
skin		
15.2.4		
redness of	Yes/No	Yes/No
the skin		
15.2.5		
blisters or	Yes/No	Yes/No
weeping skin		
15.2.6		
burning skin	Yes/No	Yes/No
15.2.7		
started within		
an hour of	Yes/No	Yes/No
contact with		
a substance		
or food item		
15.2.8		
Other?	Yes/No	Yes/No
Specify:		

☐ 53
☐ 54

☐ 55
☐ 56

☐ 57
☐ 58

☐ 59
☐ 60

☐ 61
☐ 62

☐ 63
☐ 64

☐ 65
☐ 66

Card 3

☐ 1
☐ 2

☐ 3

If YES, to any of the above go on to Question 15.3

If NO, skip to Question 15.4

15.3 Do your skin problems seem better or worse when you are away from work (for example, on weekends, off-shift and vacations)?

Give all options at once

Insert a cross (X) next to one answer only

- a) Stay the same _____
- b) Get better _____
- c) Get worse _____

15.4 Does being at work ever cause you to have any skin problems?

☐ 4

- Yes (1)
- No (2)

If YES, go on to Question 15.4.1
If NO, skip to Question 15.4.4

15.4.1 Since when have you been having these skin problems at work?

Date: Month ____ Year ____

☐☐☐☐ 5-8

15.4.2 Is there anything that you work with that makes these skin problems worse?

- Yes (1)
- No (2)

☐ 9

If YES, go on to Question 15.4.3 (**specify wheat, rye &/or premix**)
or any other substance
If NO, skip to Question 15.4.4

15.4.3 What do you think is causing these skin problems?

☐ 10

15.4.4 Have you ever bruised, burnt or injured your fingers or hands while working in the bakery?

- Yes (1)
- No (2)

☐ 11

15.5 How many times do you wash your hands in the course of a day?

☐ 12

Give all options at once
Insert a cross (X) next to one answer only

- 0 _____
- 1 time _____
- 2-3 times _____
- 4-5 times _____
- 6 or more _____

15.6 Are you using any medicines, including any creams or ointments, for your skin problems at present?

Yes (1)

No (2)

☐ 13

If YES, go on to Question 15.6.1

If NO, skip to next question 15.7

15.6.1 Which medicines?

☐ 14
☐ 15

15.7 Did you have eczema as a child?

Yes (1)

No (2)

☐ 16

Other allergic conditions

16. Are you allergic to insect stings or bites?

Yes (1)

No (2)

☐ 17

If YES, go on to Question 16.1

If NO, skip to Question 17

16.1.1-3 What kind of reactions do you have?

16.1.1 Breathing difficulty, feeling faint, fever?

Yes (1)

No (2)

☐ 18

16.1.2 Redness, itching or swelling at the sting site

Yes (1)

No (2)

☐ 19

16.1.3 Other: _____

☐ 20

17. Have you ever had any difficulty with your breathing after taking medications or injections that you did not have before?

Yes (1)

No (2)

☐ 21

If YES, go on to Question 17.1

If NO, skip to 18.1

17.1 Which medicines?

☐ 22

18.1-6 When you are near animals (such as cats, dogs or horses), near feathers (including pillows, quilts or duvets), near grass and flowers, or in a dusty part of the house, do you **ever**

18.1 Start to cough?

Yes (1)
No (2)

☐ 23

18.2 Start to wheeze?

Yes (1)
No (2)

☐ 24

18.3 Get a tight chest?

Yes (1)
No (2)

☐ 25

18.4 Start to feel short of breath?

Yes (1)
No (2)

☐ 26

18.5 Get a runny/stuffy nose or sneeze?

Yes (1)
No (2)

☐ 27

18.6 Get itchy or watery eyes?

Yes (1)
No (2)

☐ 28

18.7 Get itchy skin/rash?

Yes (1)
No (2)

☐ 29

19. Have you ever had an illness or trouble caused by eating a particular type of food/fruit?

Yes (1)
No (2)

☐ 30

If YES, go on to Question 19.1

If NO, skip to 20

19.1 What type of food/fruit was this?

☐ 31

19.1.1-6 Did this illness or trouble include:

19.1.1 Itchy skin or rash

Yes (1)

No (2)

☐ 32

19.1.2 Diarrhoea or vomiting

Yes (1)

No (2)

☐ 33

19.1.3 Runny or stuffy nose

Yes (1)

No (2)

☐ 34

19.1.4 Severe headaches

Yes (1)

No (2)

☐ 35

19.1.5 Breathlessness/tight chest/wheeze

Yes (1)

No (2)

☐ 36

19.1.6 Other: _____

☐ 37

19.2 Was the food canned or preserved?

Yes (1)

No (2)

UNK (3)

☐ 38

19.3 Do you experience these problems when you drink fizzy drinks also?

Yes (1)

No (2)

☐ 39

C. FAMILY HISTORY

1. Do/did any members of your family (blood relatives) ever have any kind of allergies?

☐ 40

Do not include relatives by marriage

If family history is completely unknown (subject is adopted, etc.), mark UNK and do not complete table. Move to next section

Yes (1)

No (2)

UNK (3)

If YES, complete table below. Insert a cross (X) in the appropriate block for each option

Type of Allergy	NO ONE in family	YES, present in the family			Do Not Know
		Parent	Brother/ Sister	Child	
1.1 Hay fever	1	2	3	4	5
1.2 Eczema	1	2	3	4	5
1.3 Asthma	1	2	3	4	5
1.4 Flour related Allergy	1	2	3	4	5
1.5 Other allergy	1	2	3	4	5
Specify:					

☐ 41

☐ 42

☐ 43

☐ 44

☐ 45

D. SMOKING HISTORY

1. Have you ever smoked tobacco (cigarettes or pipe) for as long as a year?

'YES' means at least 20 packs of cigarettes or 360 grams of tobacco in a lifetime or at least one cigarette per day for one year

Yes (1)
No (2)

☐ 46

If YES, go on to Question 1.1
If NO, skip to Question 2

1.1 How old were you when you started smoking?

_____ years old

☐ ☐ 47-48

1.2 Do you now smoke?

'YES' means smoking tobacco in the last month or more

Yes (1)
No (2)

☐ 49

If YES, go on to Question 1.2.1
If NO, skip to Question 1.3.1

1.2.1-2. How much do you now smoke on average?

1.2.1 Number of cigarettes per day _____

50-51

1.2.2 Pipe tobacco in grams/week _____

52-54

1.3. Have you stopped smoking completely?

Yes (1)

55

No (2)

If YES, go on to Question 1.3.1

If NO, skip to Question 1.4

1.3.1. How old were you when you stopped smoking completely?

_____ years old

56-57

1.3.1.1 How many years in total did you smoke cigarettes? (Do not include the years you stopped before you started again)

_____ years

58-59

1.3.2.1-2 On average of the entire time you smoked, how much did you smoke?

1.3.2.1 Number of cigarettes per day _____

60-61

1.3.2.2 Pipe tobacco in grams/week _____

62-64

1.4 Do you or did you inhale the smoke?

Yes (1)

65

No (2)

2. Have you been regularly exposed to tobacco smoke from other people smoking cigarettes or pipe in the last 12 months?

'Regularly' means on most days or nights

Yes (1)

66

No (2)

E. DIETARY HISTORY/DOMESTIC ACTIVITIES

1. How often have you eaten the following grain products in the last 12 months?

Go through each wheat product option and insert a cross (X) in the block for each option

Type of wheat product	Daily	1 to 3 times a week	1 to 3 times per month	Never
1.1 White bread/Rolls	1	2	3	4
1.2 Brown bread/Rolls	1	2	3	4
1.3 Whole wheat bread/rolls	1	2	3	4
1.4 Rye bread/rolls	1	2	3	4
2. Pastries	1	2	3	4
3. Cereals	1	2	3	4
4. Biscuits containing wheat	1	2	3	4
5. Pasta containing wheat	1	2	3	4
6. Other Specify:	1	2	3	4

Card 4

☐ 1

☐ 2

☐ 3

☐ 4

☐ 5

☐ 6

☐ 7

☐ 8

☐ 9

2. Have you changed your diet or avoided certain grain (eg. wheat/rye/soya) products because they do not agree with you when you eat them?

Yes (1)

No (2)

☐ 10

If YES, go on to Question 2.1

If NO, skip to Question 3

2.1 What grain products have you avoided?

☐ 11
☐ 12

3. Do you bake at home?

Yes (1)

No (2)

☐ 13

If YES, go on to Question 3.1

If NO, go to Question 4

3.1 How often do you do baking at home?

- a) once a month _____
- b) 2-3 times a month _____
- c) 2-3 times per week _____
- d) once a week _____
- e) everyday _____

☐ 14

3.2 What do you bake?

- a) bread/rolls _____
- b) cakes/biscuits _____
- c) tarts/pastries _____
- d) Other: _____

☐ 15
☐ 16
☐ 17
☐ 18

Specify: _____

4. Does any one else bake at home?

- Yes (1)
- No (2)

☐ 19

F. HEALTH AND SAFETY EDUCATION AND TRAINING

1. What are the hazards associated with flour dust?

☐ 20
☐ 21

2. Have you had any health and safety training on how to protect yourself when working with flour dust?

- Yes (1)
- No (2)

☐ 22

G. WORK HISTORY IN THE BAKERY INDUSTRY

1. How long have you been working at this bakery?

_____ years
_____ months

☐☐☐☐ 23-26

Present job

2. How long have you been working in your current job?

_____ years
_____ months

☐☐☐☐ 27-30

3. In which area/section are you currently working?

☐☐ 31-32

3.1 What is your job in this area/section?

Job Title _____

☐ ☐ 33-34

get a short description of the job

3.2 What products do you produce:

- | | | | |
|------------------|-----|-----|-----------------------------|
| a) doughs | Yes | (1) | <input type="checkbox"/> 35 |
| | No | (2) | |
| b) pastry | Yes | (1) | <input type="checkbox"/> 36 |
| | No | (2) | |
| c) croissants | Yes | (1) | <input type="checkbox"/> 37 |
| | No | (2) | |
| d) bread, rolls | Yes | (1) | <input type="checkbox"/> 38 |
| | No | (2) | |
| e) cakes/tarts | Yes | (1) | <input type="checkbox"/> 39 |
| | No | (2) | |
| f) biscuits | Yes | (1) | <input type="checkbox"/> 40 |
| | No | (2) | |
| g) confectionary | Yes | (1) | <input type="checkbox"/> 41 |
| | No | (2) | |
| h) other | Yes | (1) | <input type="checkbox"/> 42 |
| | No | (2) | |

Specify: _____

3.3 What ingredients do you work with?

- | | | | |
|------------------------------|-----|-----|-----------------------------|
| a) Flour (wheat, rye) | | | <input type="checkbox"/> 43 |
| | Yes | (1) | |
| | No | (2) | |
| b) Baking additives (premix) | | | <input type="checkbox"/> 44 |
| | Yes | (1) | |
| | No | (2) | |
| c) Icing sugar | | | <input type="checkbox"/> 45 |
| | Yes | (1) | |
| | No | (2) | |

d) Nuts (peanuts, hazelnuts)

Yes (1)

No (2)

☐ 46

e) Seeds (sesame, lupine)

Yes (1)

No (2)

☐ 47

f) Other

Yes (1)

No (2)

☐ 48

Specify: _____

3.4 Do you ever do other jobs during your shift on a regular basis (almost every day)?

Yes (1)

No (2)

☐ 49

If **Yes**, which jobs?

☐ 50
☐ 51

3.5 How much dust would you say your current job produces:

☐ 52

Give all options at once

Insert a cross (X) next to one answer only

a) None

b) A little

c) An average amount

d) A lot

3.5.1 What aspect of your work would you say is very dusty?

a) Tipping/Dispensing

Yes (1)

No (2)

N/A (3)

☐ 53

b) Weighing

Yes (1)

No (2)

N/A (3)

☐ 54

c) Sifting

Yes (1)

No (2)

N/A (3)

☐ 55

d) Mixing

Yes (1)
No (2)
N/A (3)

☐ 56

e) brushing table

Yes (1)
No (2)
N/A (3)

☐ 57

f) dough handling

Yes (1)
No (2)
N/A (3)

☐ 58

g) other

Yes (1)
No (2)
N/A (3)

☐ 59

Specify: _____

3.5.1.1 What type of cleaning activities in your daily work are very dusty.

3.5.1.1.1 Cleaning work table surfaces?

Yes (1)
No (2)
N/A (3)

☐ 60

3.5.1.1.2 Sweeping floors?

Yes (1)
No (2)
N/A (3)

☐ 61

3.5.1.1.3 Cleaning equipment (mixers, cutters)

Yes (1)
No (2)
N/A (3)

☐ 62

3.5.2 How far do you work from the source of the dust?

☐ 63

Give all options at once

Insert a cross (X) next to one answer only

- a) Right next to the source _____
- b) About 1-2 metres away _____
- c) More than 3 metres away _____
- d) Does not apply _____

3.6 Do you use any personal protective equipment on a regular basis (almost every day) while doing your job?

Yes (1)

No (2)

☐ 64

If NO, skip to Question 4

If YES, continue with Question 3.6.1

3.6.1 Which of the following personal protective equipment do you use on a regular basis (almost every day)?

3.6.1.1 Goggles: Yes (1)

No (2)

☐ 65

3.6.1.2 Gloves: Yes (1)

No (2)

☐ 66

3.6.1.3 Mask: Yes (1)

No (2)

☐ 67

3.6.1.4 Aprons: Yes (1)

No (2)

☐ 68

3.6.1.5 Other: _____

☐ 69

If NO to all of the previous questions, skip to Question 4

If YES to any one of the above questions, continue with Question 3.6.2.1

3.6.2.1 Goggles _____ years

☐ ☐ 70-71

3.6.2.2 Gloves: _____ years

☐ ☐ 72-73

3.6.2.3 Mask: _____ years

☐ ☐ 74-75

3.6.2.4 Aprons: _____ years

☐ ☐ 76-77

3.6.2.5 Other: _____ years

☐ ☐ 78-79

Previous jobs in present bakery

Card 5

4. Before doing this job at this bakery, did you do a different job here?

Yes (1)

No (2)

☐ 1

If NO, skip to question 5

If YES, continue with question 4.1

4.1 What other jobs did you do here?

Start with the first job and work forward, getting a one-line description of each job. If casual worker, denote each period of employment as a separate job. For continuous years of seasonal work consider as one job (provided no broken years service)

Job 1

4.1.1 Area/section _____

☐☐ 2-3

4.1.2 Job Title _____

☐☐ 4-5

get a short description of the job

4.1.3 Permanent/casual: _____

☐ 6

4.1.4. How long did you work in this job?

_____ years
_____ months

☐☐☐☐ 7-10

4.1.5 What products did you produce:

a) doughs Yes (1)

No (2)

☐ 11

b) pastry Yes (1)

No (2)

☐ 12

c) croissants Yes (1)

No (2)

☐ 13

d) bread,rolls Yes (1)

No (2)

☐ 14

e) cakes/tarts Yes (1)

No (2)

☐ 15

- f) biscuits Yes (1)
 No (2)
- g) confectionary Yes (1)
 No (2)
- h) other Yes (1)
 No (2)

☐ 16

☐ 17

☐ 18

Specify: _____

4.1.6 What ingredients did you work with?

- a) Flour (wheat, rye) Yes (1)
 No (2)
- b) Baking additives (premix) Yes (1)
 No (2)
- c) Icing sugar Yes (1)
 No (2)
- d) Nuts (peanuts, hazelnuts) Yes (1)
 No (2)
- e) Seeds (sesame, lupine) Yes (1)
 No (2)
- f) Other Yes (1)
 No (2)

☐ 19

☐ 20

☐ 21

☐ 22

☐ 23

☐ 24

Specify: _____

4.1. 7 How much dust would you say that this job produced:

☐ 25

Give all options at once
 Insert a cross (X) next to one answer only

- a) None _____
- b) A little _____
- c) An average amount _____
- d) A lot _____

4.1.8 What aspect of your work would you say was very dusty?

a) Tipping/Dispensing

Yes (1)
No (2)
N/A (3)

☐ 26

b) Weighing

Yes (1)
No (2)
N/A (3)

☐ 27

c) Sifting

Yes (1)
No (2)
N/A (3)

☐ 28

d) mixing

Yes (1)
No (2)
N/A (3)

☐ 29

e) brushing table

Yes (1)
No (2)
N/A (3)

☐ 30

f) dough handling

Yes (1)
No (2)
N/A (3)

☐ 31

g) other

Yes (1)
No (2)
N/A (3)

☐ 32

Specify: _____

4.1.8.1. What type of cleaning activities in your daily work were very dusty.

4.1.8.1.1.Cleaning work table surfaces?

Yes (1)
No (2)
N/A (3)

☐ 33

4.1.8.1.2 Sweeping floors?

Yes (1)
No (2)
N/A (3)

☐ 34

4.1.8.1.3 Cleaning equipment (mixers, cutters)

Yes (1)
No (2)
N/A (3)

☐ 35

4.1.9 How far did you work from the source of the dust?

☐ 36

Give all options at once

Insert a cross (X) next to one answer only

- a) Right next to the source _____
b) About 1-2 metres away _____
c) More than 3 metres away _____
d) Does not apply _____

4.1.10 Did you use any personal protective equipment on a regular basis (almost every day) while doing your job?

Yes (1)
No (2)

☐ 37

If NO, skip to Question 4.2.1

If YES, continue with Question 4.1.10.1

4.1.10.1 Which of the following personal protective equipment did you use on a regular basis (almost every day)?

4.1.10.1.1 Goggles: Yes (1)
No (2)

☐ 38

4.1.10.2 Gloves: Yes (1)
No (2)

☐ 39

4.1.10.3 Mask: Yes (1)
No (2)

☐ 40

4.1.10.4 Aprons: Yes (1)
No (2)

☐ 41

4.1.10.5 Other: _____

☐ 42

If NO to all of the previous questions, skip to Question 4.2.1
If YES to any one of the above questions, continue with
Question 4.1.11.1

4.1.11.1 Goggles _____ years

☐☐ 43-44

4.1.11.2 Gloves: _____ years

☐☐ 45-46

4.1.11.3 Mask: _____ years

☐☐ 47-48

4.1.11.4 Aprons: _____ years

☐☐ 49-50

4.1.11.5 Other: _____ years

☐☐ 51-52

Job 2

4.2.1 Area/section _____

☐☐ 53-54

4.2.2 Job Title _____

☐☐ 55-56

get a short description of the job

4.2.3 Permanent/casual: _____

☐ 57

4.2.4. How long did you work in this job?

_____ years
_____ months

☐☐☐☐ 58-61

4.2.5 What products did you produce:

a) doughs Yes (1)
No (2)

☐ 62

b) pastry Yes (1)
No (2)

☐ 63

c) croissants Yes (1)
No (2)

☐ 64

d) bread,rolls Yes (1)
No (2)

☐ 65

e) cakes/tarts Yes (1)
No (2)

☐ 66

f) biscuits Yes (1)
No (2)

☐ 67

- g) confectionary Yes (1)
 No (2)
- h) other Yes (1)
 No (2)

☐ 68

☐ 69

Specify: _____

4.2.6 What ingredients did you work with?

- a) Flour (wheat, rye)
 Yes (1)
 No (2)
- b) Baking additives (premix)
 Yes (1)
 No (2)
- c) Icing sugar
 Yes (1)
 No (2)
- d) Nuts (peanuts, hazelnuts)
 Yes (1)
 No (2)
- e) Seeds (sesame, lupine)
 Yes (1)
 No (2)
- f) Other
 Yes (1)
 No (2)

☐ 70

☐ 71

☐ 72

☐ 73

☐ 74

☐ 75

Specify: _____

4.2.7 How much dust would you say that this job produced:

Card 6

☐ 1

Give all options at once
 Insert a cross (X) next to one answer only

- a) None _____
 b) A little _____
 c) An average amount _____
 d) A lot _____

4.2.8 What aspect of your work would you say was very dusty?

a) Tipping/Dispensing

Yes (1)
No (2)
N/A (3)

☐ 2

b) Weighing

Yes (1)
No (2)
N/A (3)

☐ 3

c) Sifting

Yes (1)
No (2)
N/A (3)

☐ 4

d) mixing

Yes (1)
No (2)
N/A (3)

☐ 5

e) brushing table

Yes (1)
No (2)
N/A (3)

☐ 6

f) dough handling

Yes (1)
No (2)
N/A (3)

☐ 7

g) other

Yes (1)
No (2)
N/A (3)

☐ 8

Specify: _____

4.2.8.1. What type of cleaning activities in your daily work were very dusty.

4.2.8.1.1.Cleaning work table surfaces?

Yes (1)
No (2)
N/A (3)

☐ 9

4.2.8.1.2 Sweeping floors?

Yes (1)
No (2)
N/A (3)

☐ 10

4.2.8.1.3 Cleaning equipment (mixers, cutters)

Yes (1)
No (2)
N/A (3)

☐ 11

4.2.9 How far did you work from the source of the dust?

☐ 12

Give all options at once

Insert a cross (X) next to one answer only

- a) Right next to the source _____
b) About 1-2 metres away _____
c) More than 3 metres away _____
d) Does not apply _____

4.2.10 Did you use any personal protective equipment on a regular basis (almost every day) while doing your job?

Yes (1)
No (2)

☐ 13

If NO, skip to Question 4.3.1 or 5 if no other jobs

If YES, continue with Question 4.2.10.1

4.2.10.1 Which of the following personal protective equipment did you use on a regular basis (almost every day)?

4.2.10.1.1 Goggles: Yes (1)
No (2)

☐ 14

4.2.10.2 Gloves: Yes (1)
No (2)

☐ 15

4.2.10.3 Mask: Yes (1)
No (2)

☐ 16

4.2.10.4 Aprons: Yes (1)
No (2)

☐ 17

4.2.10.5 Other: _____

☐ 18

If NO to all of the previous questions, skip to Question 4.3.1 or 5
 If YES to any one of the above questions, continue with
 Question 4.2.11.1

4.2.11.1 Goggles _____ years

☐☐ 19-20

4.2.11.2 Gloves: _____ years

☐☐ 21-22

4.2.11.3 Mask: _____ years

☐☐ 23-24

4.2.11.4 Apron: _____ years

☐☐ 25-26

4.2.11.5 Other: _____ years

☐☐ 27-28

Job 3

4.3.1 Area/section _____

☐☐ 29-30

4.3.2 Job Title _____

☐☐ 31-32

get a short description of the job

4.3.3 Permanent/casual: _____

☐ 33

4.3.4. How long did you work in this job?

_____ years
 _____ months

☐☐☐☐ 34-37

4.3.5 What products did you produce:

a) doughs Yes (1)
 No (2)

☐ 38

b) pastry Yes (1)
 No (2)

☐ 39

c) croissants Yes (1)
 No (2)

☐ 40

d) bread,rolls Yes (1)
 No (2)

☐ 41

e) cakes/tarts Yes (1)
 No (2)

☐ 42

f) biscuits Yes (1)
 No (2)

☐ 43

- g) confectionary Yes (1)
 No (2)
- h) other Yes (1)
 No (2)

☐ 44

☐ 45

Specify: _____

4.3.6 What ingredients did you work with?

- a) Flour (wheat, rye) Yes (1)
 No (2)
- b) Baking additives (premix) Yes (1)
 No (2)
- c) Icing sugar Yes (1)
 No (2)
- d) Nuts (peanuts, hazelnuts) Yes (1)
 No (2)
- e) Seeds (sesame, lupine) Yes (1)
 No (2)
- f) Other Yes (1)
 No (2)

☐ 46

☐ 47

☐ 48

☐ 49

☐ 50

☐ 51

Specify: _____

4.3.7 How much dust would you say that this job produced:

☐ 52

Give all options at once
 Insert a cross (X) next to one answer only

- a) None _____
 b) A little _____
 c) An average amount _____
 d) A lot _____

4.3.8 What aspect of your work would you say was very dusty?

a) Tipping/Dispensing

Yes (1)
No (2)
N/A (3)

☐ 53

b) Weighing

Yes (1)
No (2)
N/A (3)

☐ 54

c) Sifting

Yes (1)
No (2)
N/A (3)

☐ 55

d) mixing

Yes (1)
No (2)
N/A (3)

☐ 56

e) brushing table

Yes (1)
No (2)
N/A (3)

☐ 57

f) dough handling

Yes (1)
No (2)
N/A (3)

☐ 58

g) other

Yes (1)
No (2)
N/A (3)

☐ 59

Specify: _____

4.3.8.1. What type of cleaning activities in your daily work were very dusty.

4.3.8.1.1.Cleaning work table surfaces?

Yes (1)
No (2)
N/A (3)

☐ 60

4.3.8.1.2 Sweeping floors?

Yes (1)
No (2)
N/A (3)

☐ 61

4.3.8.1.3 Cleaning equipment (mixers, cutters)

Yes (1)
No (2)
N/A (3)

☐ 62

4.3.9 How far did you work from the source of the dust?

☐ 63

Give all options at once

Insert a cross (X) next to one answer only

- a) Right next to the source _____
b) About 1-2 metres away _____
c) More than 3 metres away _____
d) Does not apply _____

4.3.10 Did you use any personal protective equipment on a regular basis (almost every day) while doing your job?

Yes (1)
No (2)

☐ 64

If NO, skip to Question 4.4.1 or 5

If YES, continue with Question 4.3.10.1

4.3.10.1 Which of the following personal protective equipment did you use on a regular basis (almost every day)?

4.3.10.1.1 Goggles: Yes (1)
No (2)

☐ 65

4.3.10.2 Gloves: Yes (1)
No (2)

☐ 66

4.3.10.3 Mask: Yes (1)
No (2)

☐ 67

4.3.10.4 Aprons: Yes (1)
No (2)

☐ 68

4.3.10.5 Other: _____

☐ 69

If NO to all of the previous questions, skip to Question 4.4.1 or 5
 If YES to any one of the above questions, continue with
 Question 4.3.11.1

4.3.11.1 Goggles _____ years

☐☐ 70-71

4.3.11.2 Gloves: _____ years

☐☐ 72-73

4.3.11.3 Mask: _____ years

☐☐ 74-75

4.3.11.4 Apron: _____ years

☐☐ 76-77

4.3.11.5 Other: _____ years

☐☐ 78-79

Job 4

4.4.1 Area/section _____

Card 7

☐☐ 1-2

4.4.2 Job Title _____

☐☐ 3-4

get a short description of the job

4.4.3 Permanent/casual: _____

☐ 5

4.4.4. How long did you work in this job?

_____ years
 _____ months

☐☐☐☐ 6-9

4.4.5 What products did you produce:

a) doughs Yes (1)
 No (2)

☐ 10

b) pastry Yes (1)
 No (2)

☐ 11

c) croissants Yes (1)
 No (2)

☐ 12

d) bread,rolls Yes (1)
 No (2)

☐ 13

e) cakes/tarts Yes (1)
 No (2)

☐ 14

f) biscuits Yes (1)
 No (2)

☐ 15

- | | | | |
|------------------|-----|-----|-----------------------------|
| g) confectionary | Yes | (1) | <input type="checkbox"/> 16 |
| | No | (2) | |
| h) other | Yes | (1) | <input type="checkbox"/> 17 |
| | No | (2) | |

Specify: _____

4.4.6 What ingredients did you work with?

- | | | | |
|------------------------------|-----|-----|-----------------------------|
| a) Flour (wheat, rye) | | | <input type="checkbox"/> 18 |
| | Yes | (1) | |
| | No | (2) | |
| b) Baking additives (premix) | | | <input type="checkbox"/> 19 |
| | Yes | (1) | |
| | No | (2) | |
| c) Icing sugar | | | <input type="checkbox"/> 20 |
| | Yes | (1) | |
| | No | (2) | |
| d) Nuts (peanuts, hazelnuts) | | | <input type="checkbox"/> 21 |
| | Yes | (1) | |
| | No | (2) | |
| e) Seeds (sesame, lupine) | | | <input type="checkbox"/> 22 |
| | Yes | (1) | |
| | No | (2) | |
| f) Other | | | <input type="checkbox"/> 23 |
| | Yes | (1) | |
| | No | (2) | |

Specify: _____

4.4.7 How much dust would you say that this job produced:

☐ 24

Give all options at once
Insert a cross (X) next to one answer only

- | | |
|----------------------|-------|
| a) None | _____ |
| b) A little | _____ |
| c) An average amount | _____ |
| d) A lot | _____ |

4.4.8 What aspect of your work would you say was very dusty?

a) Tipping/Dispensing

Yes (1)
No (2)
N/A (3)

☐ 25

b) Weighing

Yes (1)
No (2)
N/A (3)

☐ 26

c) Sifting

Yes (1)
No (2)
N/A (3)

☐ 27

d) mixing

Yes (1)
No (2)
N/A (3)

☐ 28

e) brushing table

Yes (1)
No (2)
N/A (3)

☐ 29

f) dough handling

Yes (1)
No (2)
N/A (3)

☐ 30

g) other

Yes (1)
No (2)
N/A (3)

☐ 31

Specify: _____

4.4.8.1. What type of cleaning activities in your daily work were very dusty.

4.4.8.1.1. Cleaning work table surfaces?

Yes (1)
No (2)
N/A (3)

☐ 32

4.4.8.1.2 Sweeping floors?

Yes (1)
No (2)
N/A (3)

☐ 33

4.4.8.1.3 Cleaning equipment (mixers, cutters)

Yes (1)
No (2)
N/A (3)

☐ 34

4.4.9 How far did you work from the source of the dust?

☐ 35

Give all options at once

Insert a cross (X) next to one answer only

- a) Right next to the source _____
b) About 1-2 metres away _____
c) More than 3 metres away _____
d) Does not apply _____

4.4.10 Did you use any personal protective equipment on a regular basis (almost every day) while doing your job?

Yes (1)
No (2)

☐ 36

If NO, skip to Question 5

If YES, continue with Question 4.4.10.1

4.4.10.1 Which of the following personal protective equipment did you use on a regular basis (almost every day)?

4.4.10.1.1 Goggles: Yes (1)
No (2)

☐ 37

4.4.10.2 Gloves: Yes (1)
No (2)

☐ 38

4.4.10.3 Mask: Yes (1)
No (2)

☐ 39

4.4.10.4 Aprons: Yes (1)
No (2)

☐ 40

4.4.10.5 Other: _____

☐ 41

If NO to all of the previous questions, skip to Question 5
 If YES to any one of the above questions, continue with
 Question 4.4.11.1

4.4.11.1 Goggles _____ years

☐☐ 42-43

4.4.11.2 Gloves: _____ years

☐☐ 44-45

4.4.11.3 Mask: _____ years

☐☐ 46-47

4.4.11.4 Apron: _____ years

☐☐ 48-49

4.4.11.5 Other: _____ years

☐☐ 50-51

Previous work in other bakeries

5. Have you worked in any other bakeries in the past two years?

Yes (1)

No (2)

☐ 52

If NO, skip to question 6

If YES, continue with question 5.1

5.1 Why did you change jobs?

☐ 53

5.2 What is the total amount of time you have worked in the bakery industry before you started working in this bakery?

Years _____ Months _____

☐☐☐☐ 54-57

Previous work experience

6. Name all the previous workplaces that you have worked in, when not working in this bakery or before coming to work in this bakery:

Start with the first job and work forward (including all other bakeries and jobs done)

Name of	What did	Job Title	Date	Date	Total
Company	company	(what did	start	stop	(yrs)
	make?	you do?)	(Year)	(Year)	

☐ 58

☐ 59

THANK YOU FOR ANSWERING THE QUESTIONNAIRE

APPENDIX 4

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

SPT PRETEST DATA COLLECTION SHEET

Record Number

Work number

Date

DAY				MONTH		YEAR

Card

1-3

4-9

10-15

1. Do you have any allergies that you know of? YES [1] NO [2] ☐ 16

1.1 **If Yes**, what are you allergic to? (Examples: cats, dogs, dust, grasses or trees, etc.) Please list.

☐ 17

☐ 18

☐ 19

1.2 Have you ever had a severe allergic reaction to any of these (collapse, chest tightness, wheeze)?

YES [1] NO [2] ☐ 20

If YES, indicate to the person that the skin prick tests will not be done.
Explain that a blood test will be done instead.

2. Have you ever had a severe allergic reaction to flour products (wheat/rye, premix, peanuts) (collapse, chest tightness, wheeze)?

YES (1) NO (2) ☐ 21

If YES, indicate to the person that the skin prick tests will not be done.
Explain that a blood test will be done instead.

3. Do you currently have an active skin problem such as eczema?

YES (1) NO (2) ☐ 22

If present, indicate to the person that the skin prick tests will not be done.
Explain that a blood test will be done instead.

4. Have you used any medicines or skin creams for allergies or flu in the past **3 days**?

1. YES

2.NO

☐ 23

4.1 **If yes**, which medicines?

☐ 24

☐ 25

☐ 26

If medicine contains antihistamines, indicate to the person that the skin prick tests will not be done.

Reschedule another appointment in **one** week's time and counsel accordingly.

Explain that a blood test will only be done today.

5. For Women:

5.1 Are you Pregnant?

1. YES

2.NO

☐ 27

5.2 Are you Breastfeeding?

1. YES

2.NO

☐ 28

If **Pregnant**, indicate to the person that the Skin-Prick Test will not be done today. Explain that a blood test will be done instead.

If **Breastfeeding**, proceed with Skin-Prick Testing.

6. Are you wheezing or having a tight chest today?

1. YES

2.NO

☐ 29

If YES, indicate to the person that the skin prick tests will not be done.

Explain that a blood test will be done instead.

If answers to any of the above are NO, proceed with skin prick testing.

**UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN
THE WESTERN CAPE PROVINCE OF SOUTH AFRICA
SKIN PRICK TEST DATA COLLECTION SHEET NO.1**

Card 1

Record Number

Work number

Date

						1-3
						4-9
						10-15
DAY		MONTH		YEAR		

Time started: _____

Read at (20 minutes after time started): _____

VOLAR LEFT LOWER ARM:

TOP (elbow)

Bermuda gr.	H/dust mite	BERMUDA GRASS (<i>Cynodon dactylon</i>)	HOUSE DUST MITE (<i>D. Pteronyssinus</i>)
		<div>1st diam</div> <div>2nd diam</div> <div>16-19</div>	<div>1st diam</div> <div>2nd diam</div> <div>20-23</div>
Cockroach	Rye grass	COCKROACH (<i>Blatella germanica</i>)	RYE GRASS (<i>Lolium perenne</i>)
		<div>1st diam</div> <div>2nd diam</div> <div>24-27</div>	<div>1st diam</div> <div>2nd diam</div> <div>28-31</div>
Cat	Mouldmix	CAT (<i>Felis domesticus</i>)	MOULDMIX (<i>Cladosporium herbarum</i>, <i>Alternaria alternata</i>, <i>Fusarium</i>)
		<div>1st diam</div> <div>2nd diam</div> <div>32-35</div>	<div>1st diam</div> <div>2nd diam</div> <div>36-39</div>
Dog	Grassmix	DOG (<i>Canis familiaris</i>)	GRASSMIX (<i>Pollen III - Avena, Hordeum, Triticum, Secale</i>)
		<div>1st diam</div> <div>2nd diam</div> <div>40-43</div>	<div>1st diam</div> <div>2nd diam</div> <div>44-47</div>
Aspergillus	Anisakis	ASPERGILLUS (<i>Aspergillus fumigatus</i>)	ANISAKIS (<i>Anisakis simplex</i>)
		<div>1st diam</div> <div>2nd diam</div> <div>48-51</div>	<div>1st diam</div> <div>2nd diam</div> <div>52-55</div>
- Control	+ Control	- NEGATIVE CONTROL (saline)	+ POSITIVE CONTROL (histamine)
		<div>1st diam</div> <div>2nd diam</div> <div>56-59</div>	<div>1st diam</div> <div>2nd diam</div> <div>60-63</div>

BOTTOM (wrist)

1. Other allergic symptoms/reactions during skin prick tests of left arm? (ring answer) Yes/No

64

If yes, specify? _____

2. General comment: (eg. reason test not done/ stopped, reaction to tape, dermatographism)

65

3. FIELDWORKER INITIALS: _____

66

**UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN
THE WESTERN CAPE PROVINCE OF SOUTH AFRICA
SKIN PRICK TEST DATA COLLECTION SHEET NO.2**

Card 2

Record Number

Work number

Date

						1-3
						4-9
						10-15
DAY		MONTH		YEAR		

Time started: _____

Read at (20 minutes after time started): _____

VOLAR RIGHT LOWER ARM:

TOP (elbow)

Wheat	Rye
Barley	Soya
A-amylase	Corn flour
Peanut	Oats
Storage mite	Spider mite
+ Control	- Control

WHEAT FLOUR

1 st diam	2 nd diam

1 st diam	2 nd diam

16-19

RYE FLOUR

1 st diam	2 nd diam

1 st diam	2 nd diam

20-23

BARLEY FLOUR

1 st diam	2 nd diam

1 st diam	2 nd diam

24-27

SOYA FLOUR

1 st diam	2 nd diam

1 st diam	2 nd diam

28-31

ALPHA-AMYLASE

1 st diam	2 nd diam

1 st diam	2 nd diam

32-35

CORN FLOUR

1 st diam	2 nd diam

1 st diam	2 nd diam

36-39

PEANUT (*Arachys hypogaea*)

1 st diam	2 nd diam

1 st diam	2 nd diam

40-43

OATS

1 st diam	2 nd diam

1 st diam	2 nd diam

44-47

STORAGE MITE (*Lepid. destructor*)

1 st diam	2 nd diam

1 st diam	2 nd diam

48-51

SPIDER MITE (*Tetranychus urticae*)

1 st diam	2 nd diam

1 st diam	2 nd diam

52-55

+ POSITIVE CONTROL (histamine)

1 st diam	2 nd diam

1 st diam	2 nd diam

56-59

- NEGATIVE CONTROL (saline)

1 st diam	2 nd diam

1 st diam	2 nd diam

60-63

BOTTOM (wrist)

1. Other allergic symptoms/reactions during skin prick tests of right arm? (ring answer) Yes/No

	64
--	----

If yes, specify? _____

2. General comment: (eg. reason test not done/ stopped, reaction to tape, dermographism)

	65
--	----

3. FIELDWORKER INITIALS: _____

	66
--	----

APPENDIX 5

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

LFT PRETEST DATA COLLECTION SHEET

Record Number

Work number

Date

DAY		MONTH		YEAR	

Card

1-3

4-9

10-15

1. Have you had a heart attack or stroke in the last 3 months? 1.YES 2. NO ☐₁₆

2. Do you have epilepsy? 1.YES 2. NO ☐₁₇

3. Have you had any recent operation (in the last 12 months)? 1.YES 2. NO ☐₁₈
If **Yes**, what type and how many months ago?

_____ (months)

If YES, to any of the above, indicate to the person that the lung function tests will not be done. If NO, proceed with the rest of the screening questions

4. For Women:

4.1 Are you Pregnant? 1.YES 2. NO ☐₁₉

4.2 Are you Breastfeeding? 1.YES 2. NO ☐₂₀

If **Pregnant**, indicate to the person that the Lung Function Test will not be done today.

If **Breastfeeding**, proceed with Lung Function Test with Post-Bronchodilator. Proceed with the rest of the screening questions.

5. Have you had the flu or lung infection in the past 3 weeks? 1.YES 2. NO ☐₂₁

If **Yes**, how many days ago did it end? _____ days ☐☐ ₂₂₋₂₃

6. Are you being treated for Tuberculosis? 1.YES 2. NO ☐₂₄

If **Yes**, for how long? _____ months _____ weeks ☐☐☐☐ ₂₅₋₂₈

If YES, to either question No. 5 or 6, indicate to the person that the lung function tests will not be done today. Schedule another appointment in three weeks time since the end of their illness or since the start of TB medication. If NO, continue with the rest of the questions.

7. Did you drink coffee, tea or coca-cola in the last 6 hours?

1. YES 2. NO

☐ 29

8. Have you smoked in the last hour?

1. YES 2. NO

☐ 30

If YES to No. 8, reschedule the Lung Function Test test for later the same day (at least one hour since last cigarette) or another date. Other screening procedures can be done first.

9. Have you had asthma in the past?

1. YES 2. NO

☐ 31

9.1 Do you have asthma now?

1. YES 2. NO

☐ 32

10. Are you taking any medicine/s from a doctor or clinic at the moment for your lungs, any heart condition, or your eyes?

1. YES 2. NO

☐ 33

10.1 If **Yes**, what are you taking and when did you last take them?

Names

No. of hours
since last dose

_____	_____
_____	_____
_____	_____

☐ ☐ 34-35☐ ☐ 36-37☐ ☐ 38-39

If short-acting beta-2-agonist or anti-cholinergic inhalers used in the last **4** hours or long-acting MDI or theophylline used in last **8** hours, reschedule and counsel accordingly.

11. Have you had any of the following symptoms in the past 12 months?

☐ 40

(at night, with exercise, exposure to cold air, viral infections, work exposures]

11.1 chest tightness

1. YES 2. NO

11.2 shortness of breath

1. YES 2. NO

11.3 wheezing or whistling in your chest

1. YES 2. NO

11.4 dry cough

1. YES 2. NO

12. Do you currently have any of these symptoms?

1. YES 2. NO

☐ 41

12.1 **If Yes**, which ones?

_____	_____
_____	_____

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA LUNG FUNCTION TESTS DATA COLLECTION SHEET

Record Number Card 1
 Work number
 Date

DAY			MONTH			YEAR					

1-3
4-9
10-15

1. Subject's blood pressure

systolic

[DO NOT PROCEED WITH MCT IF BP >180/110]

diastolic

2. Subject's age

YEARS
 16-17

3. Subject's gender

MALE FEMALE
 18

4.1 Subject's height

CENTIMETRES
 19-21

4.2 Subject's weight

KILOGRAMS
 22-24

5. When did you last work in the bakery?

Date 25-30

BASELINE SPIROMETRY

6. **PREDICTED FEV₁**

31-33

7. **INITIAL FEV₁ and FVC**
 (up to 8 attempts)

	FEV ₁	FVC	
1			34-39
2			40-45
3			46-51
4			52-57
5			58-63

7.1 Number of rejected attempts

64

8. **Best INITIAL FEV₁ as % of predicted FEV₁**

(divide best results from No. 7 by results from No. 6)

65-67

IF BEST INITIAL FEV₁ IS:

A) less than 60% PREDICTED or

B) less than 1.5 LITRES or

C) BP > 180/110 or

D) Breastfeeding

the individual is:

GO TO BRONCHODILATOR CHALLENGE - DO NOT DO METHACHOLINE CHALLENGE

BRONCHODILATOR CHALLENGE ONLY

9. FEV₁ and FVC

9.1 Record Best two technically satisfactory
Manoeuvres (up to 8 attempts)

FEV₁

FVC

68-73

74-79

9.2 Number of rejected attempts

--

80

METHACHOLINE CHALLENGE TEST

10. CONTROL FEV₁ following inhalation of diluent

10.1 Record two technically satisfactory manoeuvres
(up to 3 attempts)

Card 2

1-3

4-6

10.2 Number of rejected attempts

--

7

11. BEST CONTROL (post-diluent) FEV₁ as % of INITIAL FEV₁

(divide best results from No. 10 by best results from No. 7)

--	--	--

8-10

**IF BEST CONTROL FEV₁ <90% OF BEST INITIAL FEV₁ STOP METHACHOLINE CHALLENGE AND
GO TO REVERSAL OF BRONCHOCONSTRICTION**

Choice of methacholine short, medium, long protocol, standard

STOP METHACHOLINE CHALLENGE if FEV₁ falls to <80% of CONTROL FEV₁

(multiply no. 10 by 0.8)

80% of **CONTROL FEV₁**

--	--	--

12. DID THE SUBJECT ANSWER 'YES' TO QUESTIONS 9, 11 & 12
OF THE LFT Pre-Test?

NO YES

--	--

12.1 Which protocol will the subject follow?

--

11

CODING: 1 Protocol 1 (short), 2 Protocol 2 (medium), 3 Protocol 3 (long), 4 Standard Protocol

13. METHACHOLINE BATCH NUMBER

--	--	--

12-13

DOSE LEVEL	DOSE (mg of 32 mg/ml)	Best FEV ₁	2 nd Best FEV ₁	Rejected attempts	
1	Diluent	<input type="text"/>	<input type="text"/>	<input type="text"/>	14-20
2	0.0256	<input type="text"/>	<input type="text"/>	<input type="text"/>	21-27
3	0.032	<input type="text"/>	<input type="text"/>	<input type="text"/>	28-34
4	0.064	<input type="text"/>	<input type="text"/>	<input type="text"/>	35-41
5	0.128	<input type="text"/>	<input type="text"/>	<input type="text"/>	42-48
6	0.256	<input type="text"/>	<input type="text"/>	<input type="text"/>	49-55
7	0.512	<input type="text"/>	<input type="text"/>	<input type="text"/>	56-62
8	1.024	<input type="text"/>	<input type="text"/>	<input type="text"/>	63-69
9	2.048	<input type="text"/>	<input type="text"/>	<input type="text"/>	70-76

14. Why was methacholine challenge stopped?

- a) best CONTROL FEV₁ < 90% of best INITIAL FEV₁
 b) end of test reached (2.048mg of 32 mg/ml inhaled)
 c) $\geq 20\%$ fall in FEV₁ occurred
 d) subject asked to stop: reason; _____
 e) other: _____

TICK ONE BOX ONLY

<input type="checkbox"/>	1
<input type="checkbox"/>	2
<input type="checkbox"/>	3
<input type="checkbox"/>	4
<input type="checkbox"/>	5

Card 3

All participants will have a bronchodilator at the completion of the test with post-bronchodilator LFT results recorded below.

Reversal of bronchoconstriction

15. FEV₁ and FVC

15.1 Record Best two technically satisfactory manoeuvres (up to 3 attempts)

FEV ₁	FVC	
<input type="text"/>	<input type="text"/>	6-11
<input type="text"/>	<input type="text"/>	12-17

15.2 Number of rejected attempts

<input type="text"/>	18
----------------------	----

16. Best POST-BRONCHODILATOR FEV₁ as % of initial FEV₁

(divide best results from No. 14 by best results from No. 7)

<input type="text"/>	<input type="text"/>	<input type="text"/>	19-21
----------------------	----------------------	----------------------	-------

17. Has subject's FEV₁ returned to within 10% of baseline spirometry?

NO	YES	
<input type="checkbox"/>	<input type="checkbox"/>	22

IF 'YES' THE SUBJECT MAY LEAVE THE CENTRE
 IF 'NO' ADMINISTER ANOTHER 4 PUFFS OF SALBUTAMOL AND WAIT ANOTHER 10 MIN, THEN PERFORM PFT'S TO RESTORE BASELINE LUNG FUNCTION

18. FEV₁ and FVC

18.1 Record Best two technically satisfactory manoeuvres (up to 3 attempts)

FEV ₁		FVC		Card 3
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	23-28
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	29-34

18.2 Number of rejected attempts

 35

19. **Best 2nd POST-BRONCHODILATOR FEV₁ as % of initial FEV₁**

(divide best results from No. 18 by best results from No. 7)

 36-38

20. Has subject's FEV₁ returned to within 10% of baseline spirometry?

NO	YES
<input type="text"/>	<input type="text"/>

 39

All participants to answer questions below. Tick the relevant box.

21. Did the subject experience any of the following symptoms during the challenge test?

21.1 Dry or sore throat / hoarse voice

21.2 Cough

21.3 Chest tightness/wheeze/shortness of breath

21.4 Headaches/dizziness

21.1 Other

Specify _____

NO	YES
<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>

 40
41
42
43
44

22. General comments:

23. Technologist initial's _____

 45

24. Room temperature: _____
(degrees celcius)

 46-47

25 Lung function record appended

NO	YES
<input type="text"/>	<input type="text"/>

 48

APPENDIX 6

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENGLISH CONSENT FORM

1. **Title of research project**

Occupational risk factors and interventions for baker's allergy and asthma among supermarket bakery workers in the Western Cape.

2. **Purpose of the research**

The University of Cape Town is conducting this important study of the allergic effects of exposure to flour dust. This study is going to be done by researchers who are independent of the company. We will be studying a group of workers who have been involved with baking process. It is hoped that this study will provide greater insight into the risk factors for allergic sensitization among bakery workers and identify appropriate preventative strategies to be implemented in order to reduce the incidence of allergy and asthma among bakery workers.

3. **Description of the research project**

If you agree to participate you will be asked to complete the following tests during working time:

- a) **Complete a questionnaire.** A member of our study team will interview you in privacy to complete the questionnaire. You will be asked questions about any breathing or chest problems; current and previous employment history, working with flour and dietary history.
- b) **Blood test**
You will also be asked to undergo a blood test to check for allergies to specific flour allergens. Ten ml (about two teaspoons) of blood will be drawn once by a nurse.
- c) **Breathing tests**
You will be asked to blow three times into a NIOXMINO machine, which measures nitric oxide produced by the airways. This machine is used to detect if a person has allergic airway inflammation which is present in asthma or rhinitis.

4. **Confidentiality of information collected**

Your name will not appear in any reports on this study. The records of blood tests, questionnaires and breathing tests will be kept completely confidential and will be seen only by members of the study team.

5. **Risks and discomforts of the research**

- a) **From the blood tests.** You will feel a single needle stick when the blood is taken. Sometimes a small bruise may occur from the needle stick, but this is minor and will heal quickly. The total amount of blood taken is quite small and your body will quickly replace it.
- b) **From the questionnaire and breathing tests.** There are no risks from completing the questionnaire or performing the breathing test.

6. **Expected benefits to you and to others**

You will be given a written copy of all your test results along with an explanation of what they mean, unless you tell us that you do not wish to receive this. You may wish to show these to your doctor if you are having any problems. These tests will help determine if you have an allergy to flour or other substances used in the skin tests. What we learn from this study will help to protect you, and those working with flour in South Africa and other parts of the world. We will learn how best to monitor worker's health and how to reduce workers' exposure to flour allergens.

7. **Costs to you resulting from participation in the study**

The study is offered at no cost to you. In the event a problem is discovered and you wish to be seen by a doctor for it, we can recommend to you who to see. However, the study cannot pay for these additional medical visits or treatments.

8. **Contact person.**

You may contact one of the following persons for answers to further questions about the research, your rights, or any injury you may feel is related to the study.

University of Cape Town Researchers:

Prof. Mohamed Jeebhay, Telephone No. (021) 406-6309

Roslynn Baatjies, Telephone No. (021) 406-6665

University of Cape Town Research Ethics Committee:

Ms. Xolile Fula (Ethics Administrator) (021) 406-6492

**UCT OCCUPATIONAL ALLERGY AND ASTHMA AMONG
BAKERY WORKERS STUDY IN WESTERN CAPE OF SOUTH
AFRICA**

ENGLISH CONSENT FORM

STUDY NO. _____

9. Consent of the participant

I have read the information given above, or it has been read to me. I understand the meaning of this information, Dr./Mr./Ms.

_____ has offered to answer any questions concerning the study. By signing this form, I hereby consent to participate in the study. I also understand that I am free to withdraw from the study at any time without penalty.

10. Documentation of the consent

One copy of this signed document will be kept together with our research records for this study. A copy of the information sheet about the study will be given to you to keep.

Printed name of participant

Signature, Mark, or Thumb Print

Interviewer's name (Print)

Signature

DATE: _____

APPENDIX 7

University of Cape Town

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

EXHALED NITRIC OXIDE PRE-TEST DATA COLLECTION SHEET

Card 1

Survey Number _____

1-3

A. IDENTIFICATION DATA

1. Surname _____

2. First name/s _____

3. Work number _____

4-9

4. Date of birth: Day _____ Month _____ Year _____

10-15

5. Gender: Male (1)
Female (2)

16

8. Interviewer's initials _____

17

9. Date of interview: Day _____ Month _____ Year _____

18-23

10. Bakery: _____

24-25

11. Did you change your job since the last interview?

Yes (1)
No (2)
Not applicable (3)

26

11.1 If Yes or NA, what is your new job?

27-28

12. Which shift have you been working today?

04:00 - 12:00 (1)
07:00 - 16:00 (2)
08:00 - 17:00 (3)
09:00 - 18:00 (4)
12:00 - 21:00 (5)

29

B. HEALTH PROBLEMS

Recent chest infections

1. Have you had the flu or sinusitis in the past 3 weeks?

Yes (1)
No (2)

30

2. Have you had any of the following symptoms in the past **12 months** (at night, with exercise, exposure to cold air, work exposures)?

2.1 chest tightness	Yes	(1)	<input type="checkbox"/> 31
	No	(2)	

2.2 shortness of breath	Yes	(1)	<input type="checkbox"/> 32
	No	(2)	

2.3 wheezing or whistling in your chest	Yes	(1)	<input type="checkbox"/> 33
	No	(2)	

2.4 dry cough	Yes	(1)	<input type="checkbox"/> 34
	No	(2)	

2.5 Asthma	Yes	(1)	<input type="checkbox"/> 35
	No	(2)	

3. Are you being treated for Tuberculosis (TB)?			
	Yes	(1)	<input type="checkbox"/> 36
	No	(2)	

3.1 If yes, for how long?	_____ months	_____ weeks	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 37-40
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If YES, to question no 3, indicate to person that the tests will not be done today. Schedule another appointment in three months time since the start of TB medication.

Nose and eye symptoms

4. Have you ever had any nose or eye problems due to allergies and/or hay fever?

Yes	(1)	<input type="checkbox"/> 41
No	(2)	

C. SMOKING HISTORY

1. Do you smoke?

Yes	(1)	<input type="checkbox"/> 42
No	(2)	

1.1 If yes, have you smoked tobacco (cigarettes or pipe) for as long as a year?

Yes	(1)	<input type="checkbox"/> 43
No	(2)	

1.2 If yes, how many cigarettes per day do you smoke or did you smoke?	<input type="checkbox"/> <input type="checkbox"/> 44-45
--	---

1.3 Have you smoked (cigarettes/tobacco) in the last hour?

Yes (1)
No (2)

☐ 46

D. ALCOHOL CONSUMPTION

1. Do you drink alcohol?

Yes (1)
No (2)

☐ 47

1.1 If yes, when have you last consumed alcohol?

1-2 hours ago (1)
1 day ago (2)
1 week ago (3)

☐ 48

1.2 How much alcohol did you consume?

☐ 49-50

E. MEDICATION USAGE (show booklet)

1. Are you taking any medicine/s from a doctor or clinic at the moment for asthma, and or hayfever?

Yes (1)
No (2)

☐ 51

1.1 If yes, what are you taking and when last did you take them?

Names No. of hours since last dose

☐ 52-53
☐ 54-55
☐ 56-57

F. GREEN VEGETABLE CONSUMPTION

1. How often do you eat the following vegetable products?

Type of product	Daily	1 to 3 times a week	1 to 3 times per month	Never
1.1 Green salad	1	2	3	4
1.2 Spinach & other green leafy vegetables	1	2	3	4

☐ 58
☐ 59
☐ 60

2. When did you last consume green salad and/or spinach/other green leafy vegetables?

1-2 hours ago (1)
1 day ago (2)
1 a week ago (3)

☐ 61

G. PHYSICAL ACTIVITY

1. Do you exercise?

Yes (1)
No (2)

☐ 62

2. When was the last time you exercised?

1-2 hours ago (1)
1 day ago (2)
1 week ago (3)

☐ 63

H. SPIROMETRY/LUNG FUNCTION TEST

1. Have you ever had a spirometry/lung function test?

Yes (1)
No (2)

☐ 64

2. If yes, when last did you blow into a lung function machine?

1-2 hours ago (1)
1 day ago (2)
1 week ago (3)
> a week ago (4)

☐ 65

I. RECENT FOOD INTAKE

1. Did you have anything to eat or drink in the last hour?

Yes (1)
No (2)

☐ 66

If YES to above question, reschedule test for at least 1 hour later the same day or another date.

J. WORK-RELATED SYMPTOMS

1. Does being at work ever make your chest tight or wheezy?

Yes (1)
No (2)

☐ 67

2. Does being at work ever cause you to have sneezy/itchy/runny nose or red/itchy/watery eyes?

Yes (1)
No (2)

☐ 68

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

EXHALED NITRIC OXIDE DATA COLLECTION SHEET

Date: _____

Time _____

Ambient NO concentration (ppb) _____

Ambient temperature (degrees celcius) _____

Survey Number _____

[illegible]

2. Subject's age (in years) _____

3.1 Subject's height (in centimetres) _____

3.2 Subject's weight (in kilograms) _____

4. Gender: Male (1)
Female (2)

5. Effort number (start) _____

6.1 FENo measurement (ppb) 1st effort

6.2 FENo measurement (ppb) 2nd effort

6.3 FENo measurement (ppb) 3rd effort

Card 1

1-3

4-5

6-8

			9-11
			12-14

15-16

17-19

20-22

23

24-26

27-29

30-32

33-35

APPENDIX 8

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UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENVIRONMENTAL DATA COLLECTION SHEET NO. 1

A) WORKER INFORMATION

NOTE: WORKER INFORMATION SHEET TO BE COMPLETED FOR EACH WORKER SAMPLED

SURVEY NUMBER

--	--	--

1. DATE Day_____Month_____Year_____

--	--	--	--	--	--

2. BAKERY:

--	--

3. NAME: _____

4. GENDER:	MALE	1
	FEMALE	2

7

5. HAND OF PREFERENCE*: 1. LEFT
2. RIGHT
3. NO PREFERENCE

7

(*side where PAS6 sampling head should be positioned)

5. DEPARTMENT:

7

- 1 Bread bakery (dough tables)
- 2 Confectionary
- 3 Counter
- 4 Whole bakery

6. SHIFT:

1	early morning (4 - 12)
2	morning (7 - 4)
3	afternoon (12 - 8)

7

7. JOB TITLE:

9

- 1 Baker (baker assistant)
- 2 Bakery controller (supervisor)
- 3 Bakery manager
- 4 Confectioner
- 5 Counterhand
- 6 Cleaner

8. How many hours per day do you work? _____ hours

--	--

9. How many hours per week do you work?
_____ hours

--	--

10. How many years have you worked in your current job?
_____ years

--	--

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**UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG
BAKERY WORKERS IN THE WESTERN CAPE PROVINCE
OF SOUTH AFRICA**

ENVIRONMENTAL DATA COLLECTION SHEET NO. 2

WORKER TASK OBSERVATION INFORMATION

**NOTE: WORKER INFORMATION SHEET TO BE
COMPLETED FOR EACH WORKER SAMPLED**

SURVEY NUMBER _____

--	--	--

Which of the following **tasks does the worker perform?**

Weighing	1	Yes	2	No
Confectionary	1	Yes	2	No
Dough scaling	1	Yes	2	No
Dough processing	1	Yes	2	No
Operating oven	1	Yes	2	No
Counterhand	1	Yes	2	No
Cleaning	1	Yes	2	No

Did the worker **wear a mask** when performing these tasks?

Weighing	1	Yes	2	No
Confectionary	1	Yes	2	No
Dough scaling	1	Yes	2	No
Dough processing	1	Yes	2	No
Operating oven	1	Yes	2	No
Counterhand	1	Yes	2	No
Cleaning	1	Yes	2	No

UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENVIRONMENTAL DATA COLLECTION SHEET NO. 3

DUST MEASUREMENTS WITH PAS-6 SAMPLING HEAD

NOTE: COMPLETED FOR EACH WORKER SAMPLED

--	--	--

PUMP NO.	
PAS6 HEAD NO.	
SAMPLE NO.	
FILTER NO.	
START TIME	
END TIME	
DURATION (MINS)	
FLOW RATE (PRE)	litres
FLOW RATE (POST)	litres

GENERAL COMMENTS:

APPENDIX 9

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ACKNOWLEDGEMENTS

This manual has been compiled by Ms R Baatjes and Prof MF Jeebhay of the Occupational and Environmental Health Research Unit, University of Cape Town. This manual is a translated adaptation of a Dutch dust control manual compiled by TNO and Industox as part of a large health surveillance scheme in the Netherlands (<http://www.blijmetstofvrij.nl>). We would like to acknowledge the contributions of Mr T Meijster (TNO & Institute of Risk Assessment Sciences) and the Health and Safety Executive (United Kingdom) with regard to the text and some of the illustrations used in this publication. We are also grateful to Ms Magda Schinkel for assistance with the translation. Funding for the development of this manual has been obtained from the Medical Research Council, Department of Trade and Industry (THRIPP), National Research Foundation and the University of Cape Town.

DUST CONTROL IN THE BAKERY
MANUAL





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ACKNOWLEDGEMENTS BACK COVER

SECTION 1

INTRODUCTION

1.1 WHY THIS MANUAL?

You may well know that it is not only chemicals, but also dusts of natural origin that can lead to complaints or illness. Everybody knows someone in his or her direct surroundings, with for example, hay fever or an allergy to particular pets. These complaints or illnesses are caused by so-called allergens. These allergens are substances (proteins), to which the body, after repeated contact, reacts strongly (allergic reaction) causing inflammation (swelling) or narrowing of the airways. There are allergens even in flour and bread improvement products to which you can develop an allergic reaction should you come into contact with these products. Regular contact with flour or additives can lead to irritation of the upper airways, asthma (baker's asthma) or skin eczema (baker's dermatitis). These illnesses can lead to workers having to take sick leave leading to a negative impact on their productivity. Furthermore, workers with long term problems could eventually be forced to find another occupation. This manual has been written in order to prevent complaints or illness as a result of exposure to flour (dust) and other ingredients used in bread and confectionery products.

The manual describes measures that you can introduce to prevent or reduce the exposure to flour (dust) and other ingredients used in the bakery.

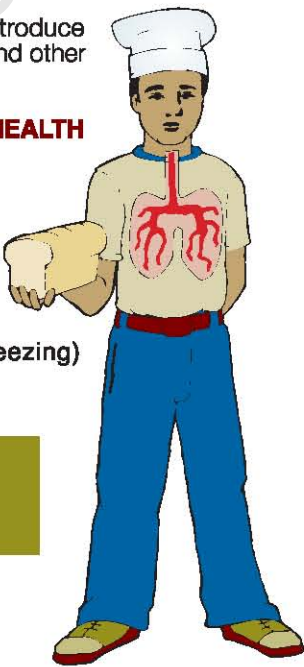
1.2 MORE INFORMATION ON FLOUR DUST & HEALTH PROBLEMS

What is the problem?

Flour and bakery dust if not handled properly can cause:-

- Baker's asthma (occupational asthma)
- Eye irritation (itchiness, red eyes, teariness)
- Nose irritation (itchiness, runny nose, sneezing)
- Skin problems (itchiness, skin rash)

Research done in supermarket bakeries in Cape Town show that one out of every 10 bakers (10%) has baker's asthma.



What is baker's asthma?

Asthma is a common lung disease that makes breathing difficult. When it is caused by breathing in hazardous substances in the workplace, it is called occupational asthma. The name *"baker's asthma"* is commonly used to describe occupational asthma in bakery employees. If you work in a bakery or similar workplace, you are at risk of getting asthma. Asthma can affect your ability to work and your overall quality of life. It can even be life threatening.

What are the symptoms of baker's asthma?

People suffering from baker's asthma often do not realize that their symptoms are work-related. The symptoms of baker's asthma are the same as for common asthma.

They include some or all of the following:

- wheezing
- chest tightness
- shortness of breath
- cough at night

With baker's asthma, however, the symptoms usually become worse during the working day and throughout the workweek. The symptoms decrease and may be totally absent on days off work and during vacations.



What causes baker's asthma?

Baker's asthma is caused by breathing in flour dust and other substances (allergens) commonly found in bakeries and similar workplaces. Table 1 lists some examples.

TABLE 1: SUBSTANCES (ALLERGENS) KNOWN TO CAUSE BAKER'S ASTHMA	
ASTHMA-CAUSING SUBSTANCES	EXAMPLES
Flour and grains	wheat, rye, barley, soy or buckwheat
Enzymes that are added to improve the bread quality	alpha-amylase, protease, xylanase
Other additives	eggs or egg powder, sesame seeds, nuts, mites and moulds

SECTION 2

2. FLOUR DUST EXPOSURES IN BAKERIES

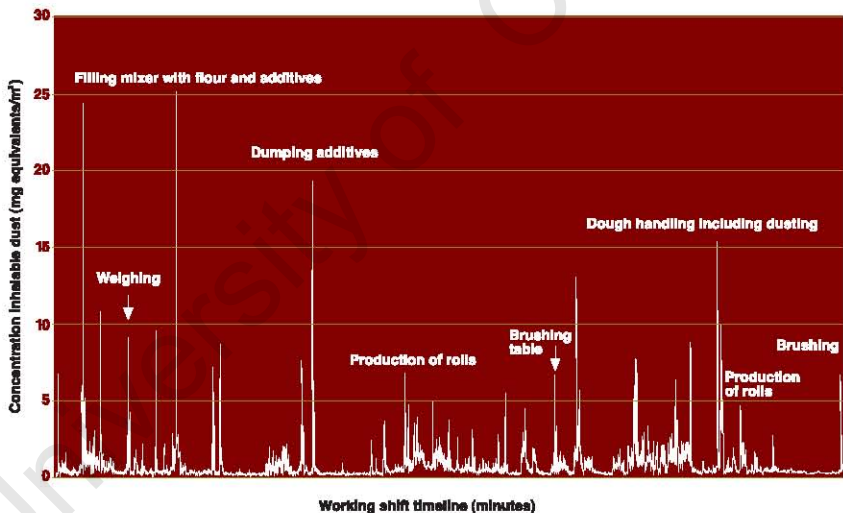
2.1 INTRODUCTION

With exposure, we mean the contact between flour (dust) and the worker in the bakery. Exposure can take place through breathing in dust, through contact with the skin and/or through eating. When the hands become contaminated with dust it can, through rubbing or scratching, spread to other parts of the body, amongst others, the eyes.

2.2 TASKS AND PEAK (HIGH) EXPOSURES

The flour dust concentration as well as the exposure can be measured with certain measuring equipment during a working day. Figure 1 shows the results that are given by such a measuring device.

Figure 1. Tasks and peak flour (dust) exposures



From Figure 1 it can be seen which activities/tasks cause high exposures (peak exposure). Especially during weighing, pouring of flour and additives, dusting with flour, and cleaning activities (dry sweeping) high dust exposure can occur. Between the peaks the exposure is negligible (much lower). If the tasks/activities that lead to high exposures are controlled then the daily exposure experienced by the worker will decrease.

EXAMPLES OF ACTIVITIES THAT CAUSE HIGH FLOUR DUST EXPOSURES



EXAMPLE OF ACTIVITIES WITH LOW FLOUR DUST EXPOSURES



It is evident that the job of the worker in the bakery will influence the exposure. Generally, a confectioner will have a lower personal flour exposure than a bread baker. This is mainly due to the confectioner performing activities with less flour and baking additives. If different workers in the bakery have different tasks, (for instance one person prepares mainly dough, while someone else works with the oven), then the exposure of these workers would also be different, unless they are working very close to each other.

Research studies of supermarket bakeries in Cape Town show that bakers, on average, have twice as high flour dust exposures compared to confectioners. Counterhands, on the other hand, have the lowest exposures, almost half that of confectioners.

2.3 WORKING PRACTICES

The manner of working has a large influence on the extent of the exposure. An example is shaking the bags to empty. The shaking of bags differs per bakery and per person. If the worker shakes the bag vigorously to ensure that all the flour is removed, more dust will arise than when a bag of flour is carefully emptied. Dusting the work-table with flour from high above the work-table, leads to higher dust levels than rubbing the work-table with flour. Although this is perhaps not always possible because of increasing workloads, you can through gentle and careful working, significantly decrease exposure to flour dust.

SECTION 3

3.1 FLOUR DUST CONTROL: MAIN MESSAGES

THE 10 TOP HINTS

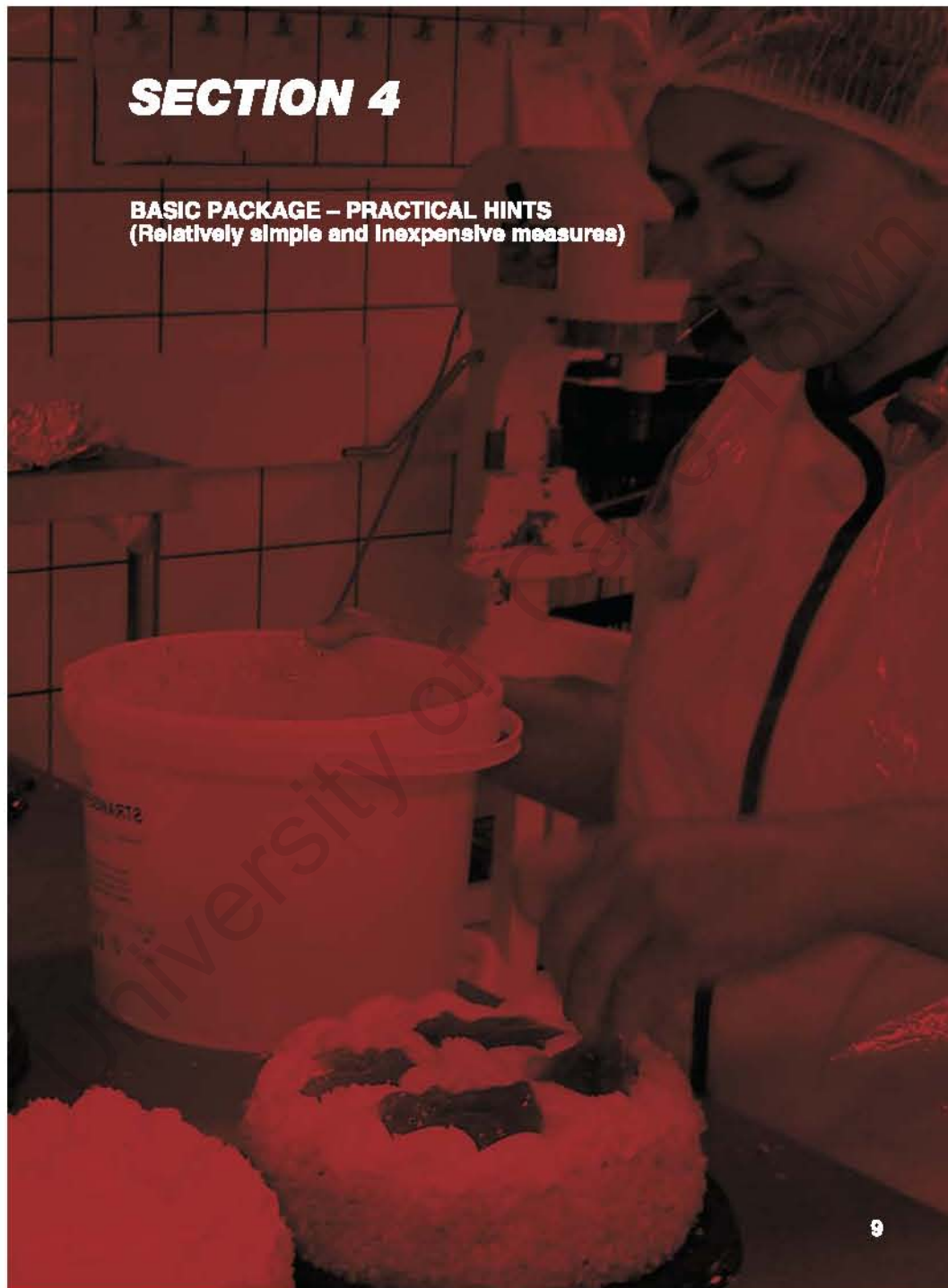
- 1 **Avoid damage to** ingredient **bags**.
- 2 **Avoid spillages** of flour where possible and where spillages do occur clean up immediately.
- 3 Take care to **avoid airborne dust** while **loading** ingredients into mixers. **Do not shake bags when emptying**.
- 4 **Minimise** the creation of **airborne dust** when **folding** and **disposing of** empty bags. One effective method is to roll the bag up from the bottom while tipping, thereby avoiding the need to flatten or fold empty bags.
- 5 **Start up mixers on slow speed** until wet and dry ingredients form a mixture.
- 6 **Use dredgers or sprinklers** for dusting the work-table rather than hand throwing of flour.
- 7 Handle flour and powdered products carefully. **Minimise the use of dusting flour**, or use oil where appropriate. Dropping flour from a height or throwing with force will cause dust to remain airborne.
- 8 **Wear a suitable mask** for any essential **short term dusty tasks**.
- 9 **Do not use compressed air/lines for cleaning**.
- 10 **Do not** use brushes to **dry sweep** dust as they cause high levels of airborne dust. **Use high** efficiency industrial **vacuum cleaners** for general cleaning. Shovel up large amounts gently.

3.2 FLOUR DUST CONTROL CHART

	STEPS IN THE PROCESS	BASIC PACKAGE	
		DUST CONTROL METHOD	CONTENTS
S T E P I N P R O C E S S	STORAGE AND WEIGHING OF RAW MATERIALS	1	Dust free procedures for storage, pre-treatment & supplies
		2	Method of opening and emptying of bags
		3	Method of weighing of raw materials
	DOUGH PREPARATION	2	Method of opening and emptying of bags
		4	Dust free methods of dough preparation
	DOUGH PROCESSING	5	Dust free methods for dough processing (moulding, dividing) or using a dough brake
	USE OF PERSONAL PROTECTIVE EQUIPMENT	6	Use of personal protective equipment - breathing protection
		7	Use of personal protective equipment - skin protection & work clothing
	CLEANING	8	Dust control methods during cleaning activities
		9	Industrial vacuum cleaners

SECTION 4

BASIC PACKAGE – PRACTICAL HINTS
(Relatively simple and inexpensive measures)



DUST CONTROL METHOD 1

DUST FREE PROCEDURES FOR STORAGE, PRE-TREATMENT AND SUPPLIES

General

- Prevent damage to bags (packaging) during delivery.
- Hold reserve bags close by to avoid damage to bags.
- Avoid dust creation by limiting the throwing and dragging of bags – the external surface of the bags can contain a lot of dust.
- Try, where possible, to purchase single dose packets or use whole bags, so that the ingredients do not need to be weighed.
- By careful movement of bags, avoid obstruction of walking areas where possible.
- Clean spilled raw materials immediately (see control method 8).

Practical hints

- Use, where possible, a handheld pallet trolley for moving bags to limit dragging of bags.
- If raw materials are manually poured from bags, then bags must be opened in accordance with the prescribed methods, emptied and removed (see control method 2).



Example of dust due to damage to bags

DUST CONTROL METHOD 2

METHOD OF OPENING AND EMPTYING OF BAGS

Practical hints

Prescribed methods for the opening and emptying of bags:

- Cut the bag open at the top.
- Place the bag with the opening close to the bottom of the mixer with the flap closed. Ensure that the dispensing height is as low as possible.
- Lift the bag so that the flour can pour out of the bag.
- Do not shake the bag at all.
- Once the bag is empty, carefully remove the bag and ensure that the flap is closed.
- Keep the flap in a closed position when adding the other ingredients (e.g. premix)
- Fold or roll the empty bag carefully. The clearing of empty bags can lead to high dust exposure.
- Remove all empty and used packaging carefully (take care that no dust is created in the process).



DUST CONTROL **METHOD 3**

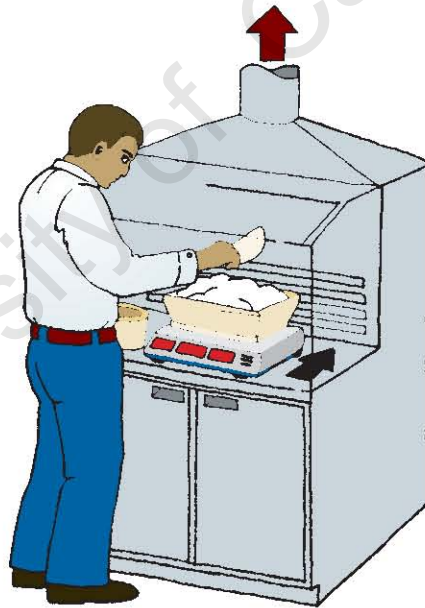
METHOD OF WEIGHING RAW MATERIALS

Practical hints

- Weigh raw materials in a weighing cabin with exhaust, if available.
- Weigh raw materials carefully with a scoop.
- Place the scale on a work-table. Avoid the use of a scale that is placed at eye height, because the dust that arises will be in the immediate breathing zone of the worker.

More Information

- Clean: Clean the scale and work-table immediately after use, or at the end of each working day. Clear any spilt products immediately, and use respiratory protection if large quantities are spilt (**see control method 6 & 8**).



Example of a weighing cabin with exhaust

DUST CONTROL *METHOD 4*

DUST FREE METHODS OF DOUGH PREPARATION

Practical hints

- Add water carefully, along the wall of the mixer. Empty buckets carefully or use a hosepipe.
- Start the mixer on a low speed.
- Place the exhaust directly above the mixer if present.
- Check if closure of the lid and flap on the mixer (if present) is adequate when adding flour and ingredients.



DUST CONTROL **METHOD 5**

DUST FREE METHODS FOR DOUGH PROCESSING (MOULDING, DIVIDING) OR USING A DOUGH BRAKE

Practical hints

- Reduce airborne flour dust as much as possible.
- Use no more dusting flour on work-table than necessary.
- Avoid spills and work gently.
- Divide the flour by hand or use a sieve to dust work-table with flour. Less dust is produced in comparison to when the flour is scattered from high above the work-table (see pictures).
- Use a non-stick table surface for example a work-table made of polyethylene, rust-free/stainless steel or aluminium.
- Use a Teflon-coating on the ball forming sheets for small bread or rolls (more expensive measure).



Dusting work table with flour from high above the surface increases exposure to flour dust (picture above). Using a sieve or rubbing surface with flour creates less dust (picture below)



DUST CONTROL **METHOD 6**

USE OF PERSONAL PROTECTIVE EQUIPMENT – BREATHING PROTECTION

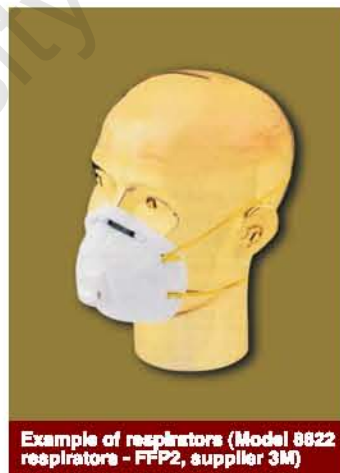
General

Personal protective equipment, such as a dust mask or gloves, are rarely used in bakeries. Yet, there are activities, through which the use of personal protection would be a good measure to prevent exposure. However, personal protection should only be used, when other control measures, such as substitution by a less dusty process or local exhaust ventilation cannot be achieved, or when high exposure to dust is expected due to incidental activities (such as maintenance work).

Examples of activities during which high exposures can be expected, are:

- manual pouring of various bags of raw material (flour and/or additives)
- clearing of large quantities of spilt flour
- maintenance or cleaning of machinery (e.g. pastry crust roller)

Note: The use of personal protection does not mean that the exposure will automatically be lower. Wearing of old contaminated masks or the use of an old filter in a respiratory protection mask can increase the exposure.



Example of respirators (Model 8822 respirators - FFP2, supplier 3M)

Practical hints

- Use a FFP2 dust filter (disposable or half face, see picture) only for tasks of a short duration (dust creation), such as the cleaning of small quantities of spilt flour.





More Information

- Maintenance: Exchangeable dust filters need to be replaced in the following manner:
 - daily at high exposure
 - twice per week at average exposure
 - once every 2 weeks at low exposure
- Storage: Store the respiratory protective equipment in a specific place where it will not be exposed to dust, refuse or chemicals.
- Information: careful instruction and training must be given to workers regarding the correct use, maintenance and storage of breathing protective equipment (see fitting instruction pictures).

Draw back / Important to take into account

- A disadvantage of dust masks is that they can be annoying when working in hot environments.
- Facial hair (beard) may interfere with the effectiveness of the mask.

FITTING INSTRUCTION FOR RESPIRATOR USE

	<div>1</div> <p>Cup the respirator in your hand with the nosepiece at your fingertips allowing the headbands to hang freely below your hand.</p>
	<div>2</div> <p>Position the respirator under your chin with the nosepiece up.</p>
	<div>3</div> <p>Pull the top strap over your head resting it high at the top back of your head. Pull the bottom strap over your head and position it around the neck below the ears.</p>
	<div>4</div> <p>Place the fingertips of both hands at the top of the metal nosepiece. Mould the nosepiece to the shape of your nose by pushing inward while moving your fingertips down both sides of the nosepiece. Pinching the nosepiece using one hand may result in less effective respirator performance.</p>
	<div>5</div> <p>The seal of the respirator on the face should be fit-checked prior to wearing in the work area.</p> <div><div>a)</div><div>Cover the front of the respirator with both hands, being careful not to disturb the position of respirator. Inhale sharply. A negative pressure should be felt inside the respirator. If any leakage is detected, adjust position of respirator and/ or tension of strap. Retest the seal. Repeat the procedure until the respirator is sealed properly.</div></div> <div><div>b)</div><div></div></div>

DUST CONTROL *METHOD 7*

USE OF PERSONAL PROTECTIVE EQUIPMENT - SKIN PROTECTION AND WORK CLOTHING

General

- Keep work and private-clothing separately (where possible) and avoid clothing from contaminating the non bakery space.
- During construction and new development it is advisable to build a separate space for work and private clothing and a shower.
- Retain the flour dust in the bakery, by ensuring that work clothes are removed at the bakery and that workers can shower if possible after the shift.

Practical hints

- Use suitable (for instance nitrile rubber, not cotton) and good fitting gloves, during activities involving contact with flour and additives such as bread improver.
- Handle gloves carefully during fitting and removal.
- Wear the prescribed baker's work clothing.
- Wash work clothing after each working day (minimal 60 degrees Celcius).
- Use disposable gloves once only.
- Replace broken gloves immediately.
- Store gloves in a clean dedicated space, free from dust, refuse/dirt or chemicals.

More information

- Educate and train workers regarding the correct use, maintenance and storage of work clothing and gloves.

DUST CONTROL **METHOD 8**

DUST CONTROL METHODS DURING CLEANING ACTIVITIES

General

By good housekeeping practices you can reduce exposure to flour dust substantially. A clean workplace will lead to less dust exposure.

- Ensure that employees have facilities to wash before breaks and after work.
- Ensure that employees wear work clothing and do not take these home
- Clean the work space, including equipment and tools, daily using wet methods (water, damp cloth etc) instead of dry methods such as sweeping and brushing.
- Clean the dough table after use.
- Clean general spaces, ceiling beam, pipe systems and light installations weekly.



Example of good hygiene practices, using damp cloth to clean work surface

- As far as possible limit the use of a broom and/or hand sweeper (dry techniques)
- Clean flour spills and/or other raw materials immediately. Clear large quantities carefully by means of a scoop and refuse bag. Use respiratory protection during this process (**see control method 6**).
- Develop cleaning schedules. Develop a cleaning schedule indicating who cleans, what, when (also Hazard Analysis Critical Control Point (HACCP) - requirement).

Practical hints

- Clean where possible using wet methods - for instance with a wet cloth or a mop.
- Use a rubber broom to reduce dust formation (see picture).
- If you have an industrial vacuum cleaner, use a special HEPA-filter suitable for the capturing of small dust particles). Or get one!!

More information

Maintenance: Vacuum cleaner filters and bags must be regularly checked and replaced where necessary (see control method 9).



DUST CONTROL **METHOD 9**

INDUSTRIAL VACUUM CLEANERS

General

- Use an industrial vacuum cleaner for cleaning of the bakery, including equipment, to prevent dust exposure.
- The vacuum cleaner must contain a **HEPA filter (High Efficiency Particulate Air Filter)**, so that all dust particles can be captured.
- Vacuum cleaner filters and bags must be checked and replaced regularly.
- Follow the instructions of the vacuum cleaner (as indicated in the supplier's manual).



Sweeping of flour dust increases "dustiness", which is best avoided by use of an industrial vacuum cleaner



Example of an industrial vacuum cleaner

APPENDIX 10

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UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

ENVIRONMENTAL DATA COLLECTION SHEET NO. 1

A) WORKER INFORMATION

NOTE: WORKER INFORMATION SHEET TO BE COMPLETED FOR EACH WORKER SAMPLED

SURVEY NUMBER

--	--	--

1. DATE Day_____Month_____Year_____

--	--	--	--	--	--

2. BAKERY: _____

11/11

3. NAME: _____

4. GENDER:	MALE	1
	FEMALE	2

9

5. HAND OF PREFERENCE*: 1. LEFT
2. RIGHT
3. NO PREFERENCE

(*side where PAS6 sampling head should be positioned)

5. DEPARTMENT:

9

- 1 Bread bakery (dough tables)
- 2 Confectionary
- 3 Counter
- 4 Whole bakery

6. SHIFT:

1	early morning (4 - 12)
2	morning (7 - 4)
3	afternoon (12 - 8)

7. JOB TITLE:

11

- 1 Baker (baker assistant)
- 2 Bakery controller (supervisor)
- 3 Bakery manager
- 4 Confectioner
- 5 Counterhand
- 6 Cleaner

8. How many hours per day do you work? _____ hours

--	--

9. How many hours per week do you work?
_____ hours

--	--

10. How many years have you worked in your current job?
_____ years

--	--

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**UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG
BAKERY WORKERS IN THE WESTERN CAPE PROVINCE
OF SOUTH AFRICA**

ENVIRONMENTAL DATA COLLECTION SHEET NO. 2

WORKER TASK OBSERVATION INFORMATION

**NOTE: WORKER INFORMATION SHEET TO BE
COMPLETED FOR EACH WORKER SAMPLED**

SURVEY NUMBER _____

--	--	--

Which of the following **tasks does the worker perform?**

Weighing	1	Yes	2	No
Confectionary	1	Yes	2	No
Dough scaling	1	Yes	2	No
Dough processing	1	Yes	2	No
Operating oven	1	Yes	2	No
Counterhand	1	Yes	2	No
Cleaning	1	Yes	2	No

Did the worker **wear a mask** when performing these tasks?

Weighing	1	Yes	2	No
Confectionary	1	Yes	2	No
Dough scaling	1	Yes	2	No
Dough processing	1	Yes	2	No
Operating oven	1	Yes	2	No
Counterhand	1	Yes	2	No
Cleaning	1	Yes	2	No

**UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG
BAKERY WORKERS IN THE WESTERN CAPE PROVINCE
OF SOUTH AFRICA**

ENVIRONMENTAL DATA COLLECTION SHEET NO. 3

DUST MEASUREMENTS WITH PAS-6 SAMPLING HEAD

NOTE: COMPLETED FOR EACH WORKER SAMPLED

SURVEY NUMBER _____

PUMP NO.	
PAS6 HEAD NO.	
SAMPLE NO.	
FILTER NO.	
START TIME	
END TIME	
DURATION (MINS)	
FLOW RATE (PRE)	litres
FLOW RATE (POST)	litres

GENERAL COMMENTS:

APPENDIX 11

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UCT OCCUPATIONAL ALLERGY AND ASTHMA STUDY AMONG BAKERY WORKERS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA

IMPLEMENTATION OF INTERVENTION IN BAKERY - CHECKLIST

A. IDENTIFICATION DATA

1. Bakery: _____

☐ ☐

2. Inspection done by: _____

☐ ☐

3. Date of inspection:
Day _____ Month _____ Year _____

☐ ☐ ☐ ☐ ☐ ☐

4. Intervention group category:

- Lid & Manual (1)
Manual only (2)
Control (3)

☐

B. CONTROL METHOD 1

Storage of products

1. Are bags damaged causing flour dust exposure (flour spillages)?



- Yes (1)
No (2)
N/A (3)

☐

2. Are reserve bags held closely to avoid damage to bags?

- Yes (1)
No (2)
N/A (3)

☐

CONTROL METHOD 2

Method of opening and emptying bags

1. Does the mixing tub have a lid (intervention lid)?

- Yes (1)
No (2)
N/A (3)

☐

1.1. If yes, condition of lid (being used/broken/been replaced)?



1.2 If yes, are bags placed in opening to dispense flour?

- Yes (1)
No (2)

☐



1.3 Are premixes added through the opening as in picture?

- Yes (1)
No (2)

☐


1.4 Are bags emptied as in picture, causing dust exposures?

- Yes (1)
No (2)
N/A (3)

☐

CONTROL METHOD 5

Dust free methods for dough processing:

1. Are workers dusting work tables from high positions (see picture)?



- Yes (1)
No (2)
N/A (3)

☐

2. Are any one of the following methods used (to reduce dust exposure)?



2.1 Rubbing table with flour?

- Yes (1)
No (2)
N/A (3)

☐


2.2 Using a sieve to dust table?

- Yes (1)
No (2)
N/A (3)

☐


2.3 Using oil instead of flour?

- Yes (1)
No (2)
N/A (3)

☐

2.3.1 If yes, or which products is oil being used?

CONTROL METHOD 6

Use of personal protective equipment

1. Are appropriate PPE available in the bakery (FFP2 masks).



Yes	(1)
No	(2)
N/A	(3)

☐

2. Are the guidelines for wearing PPE followed by workers?

Yes	(1)
No	(2)
N/A	(3)

☐

3. Are PPE used for the following tasks?

3.1 Manual pouring of flour into mixer?

Yes	(1)
No	(2)
N/A	(3)

☐

3.2 Cleaning and clearing of large quantities of split flour?

Yes	(1)
No	(2)
N/A	(3)

☐

3.3 Maintenance or cleaning of machinery?

Yes	(1)
No	(2)
N/A	(3)

☐

CONTROL METHOD 8/9

Dust control during cleaning activities

1. Are wet methods used (hosing, wet towels, mopping?)



Yes	(1)
No	(2)
N/A	(3)

☐

2. Are dry methods used (sweeping, brushing)?

Yes	(1)
No	(2)
N/A	(3)

☐

2.1 If yes, please indicate which method is used, see pictures.



2.1.1 Normal broom?

- Yes (1)
No (2)
N/A (3)

☐


2.1.2 Microfibre mop

- Yes (1)
No (2)
N/A (3)

☐

2.1.3 Other

- Yes (1)
No (2)
N/A (3)

☐

Specify: (eg. rubber broom) _____

3. Are industrial vacuum cleaners present in bakeries?



- Yes (1)
No (2)
N/A (3)

☐

3.1 If yes, are vacuum cleaners being used by the worker?

- Yes (1)
No (2)

☐

3.2 If NO to above question, why not?

☐

COMMENTS REGARDING OBSERVATIONS MADE:



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